



Spaceflight Associated Neuro-ocular Syndrome (SANS)

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Deep Space Gateway Symposium
4 Dec 2017



History

Hyperopic Shifts

-Up to +1.75 diopters

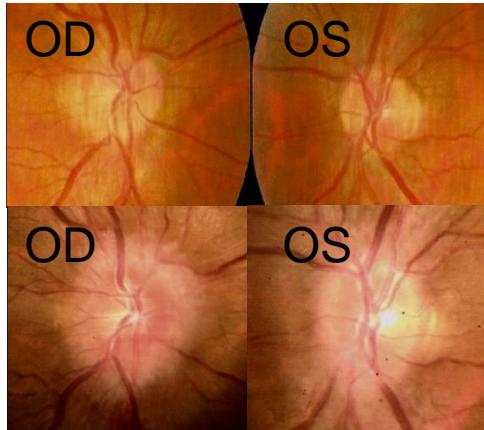


“Cotton wool” spots



Risk: Visual Impairment/Intracranial Pressure (VIIP)

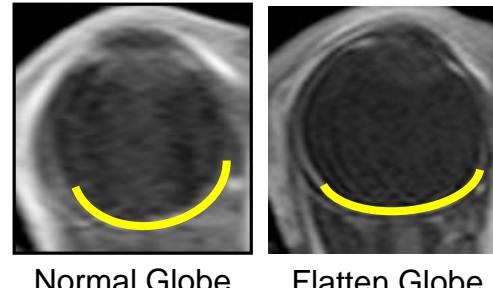
Optic Disc Edema (swelling)



Choroidal Folds



Globe Flattening

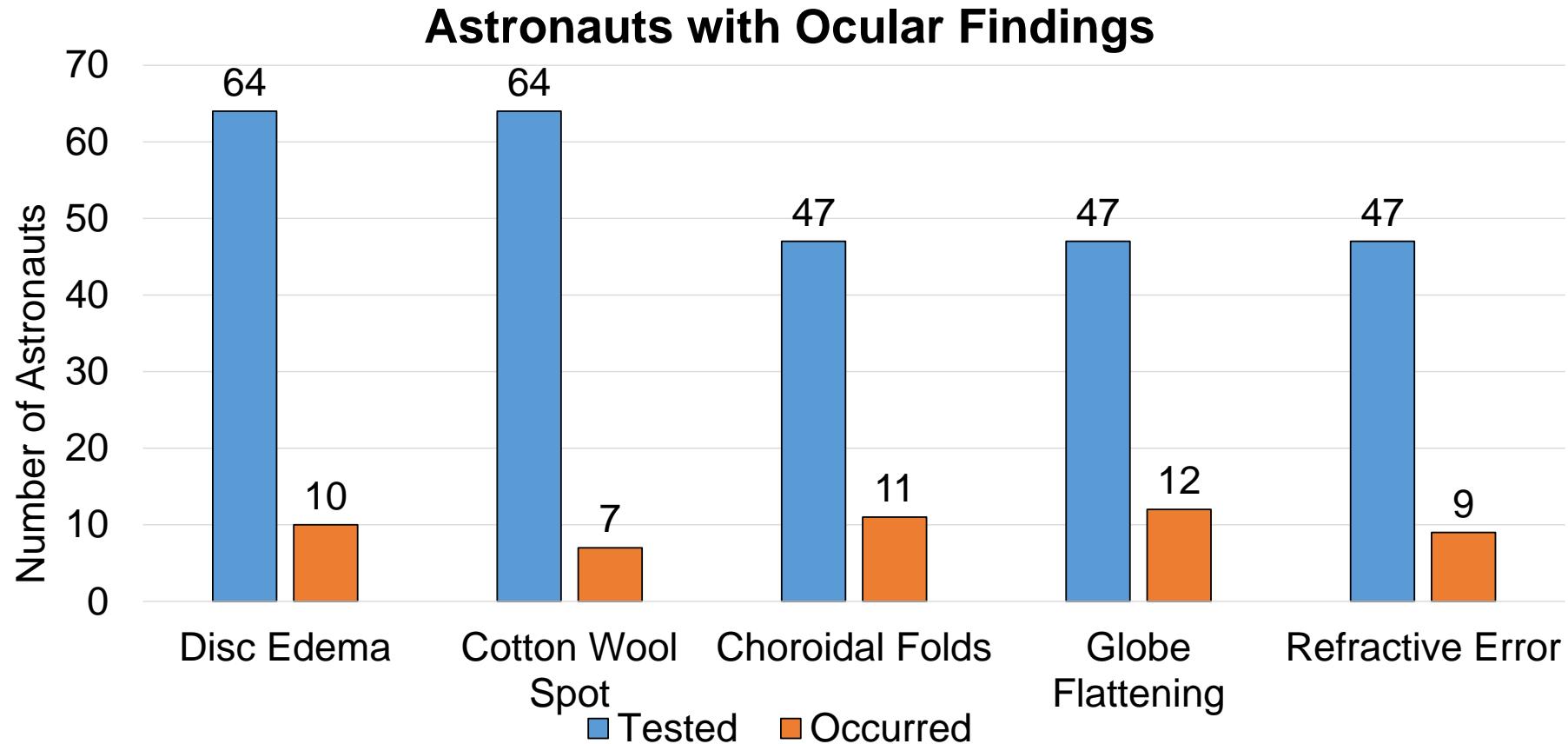


Normal Globe

Flatten Globe



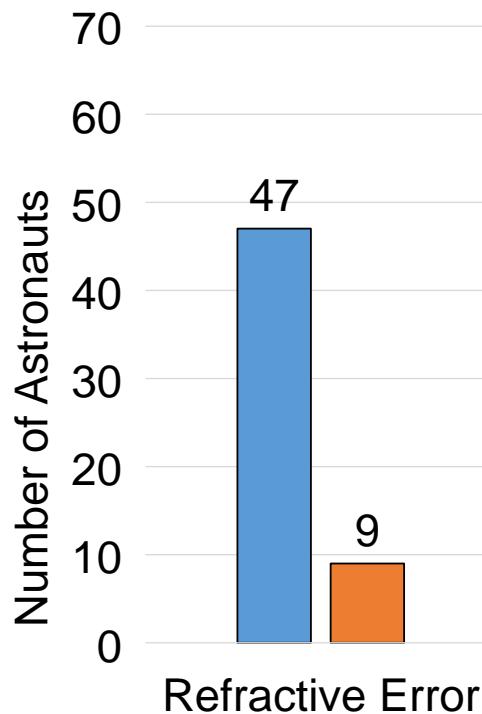
Ocular Findings through 2016*



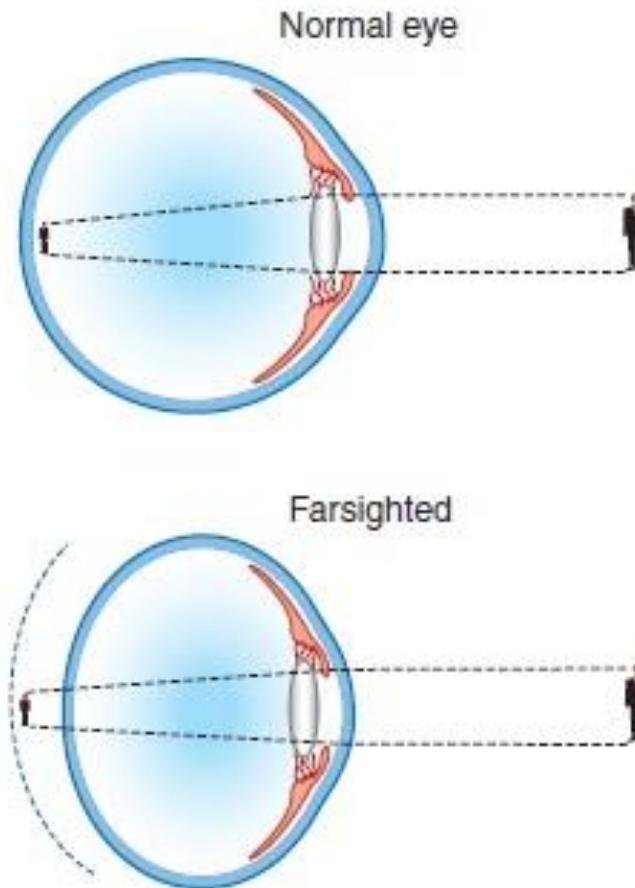
*USOS astronauts only 3



Refractive Error

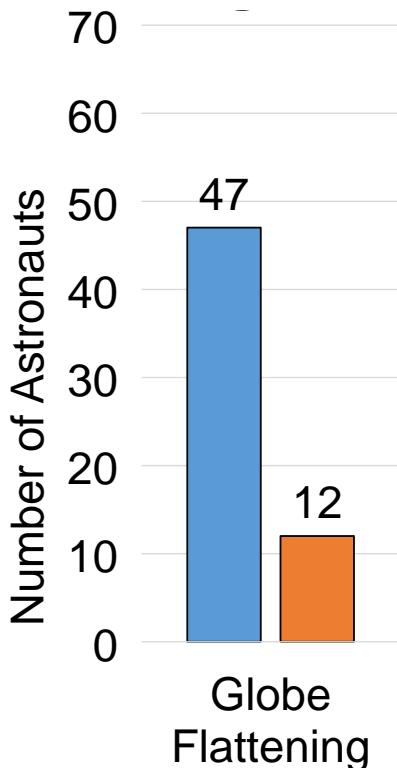


Change $\geq 0.75\text{D}$

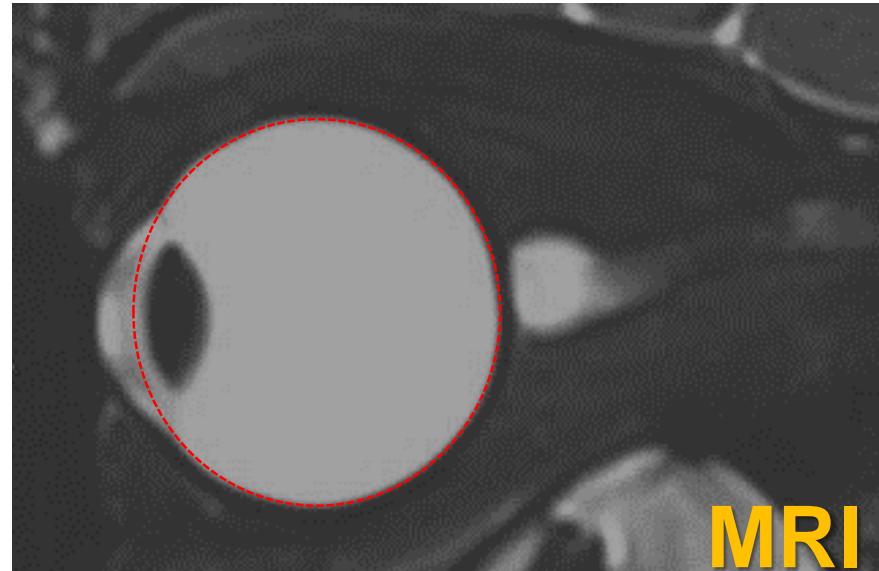




Globe Flattening



Terrestrially: Globe flattening is associated with disc edema resulting from intracranial hypertension.

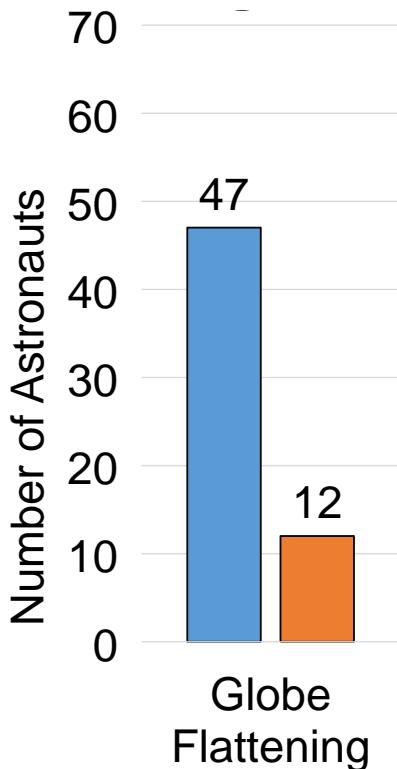


Pre-flight

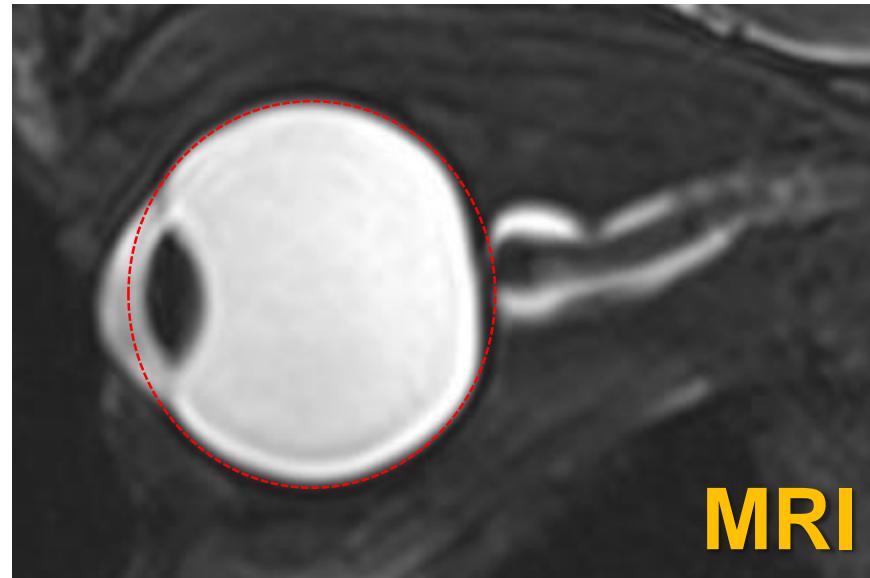
Subjective call from
MRI, ultrasound



Globe Flattening



Terrestrially: Globe flattening is associated with disc edema resulting from intracranial hypertension.

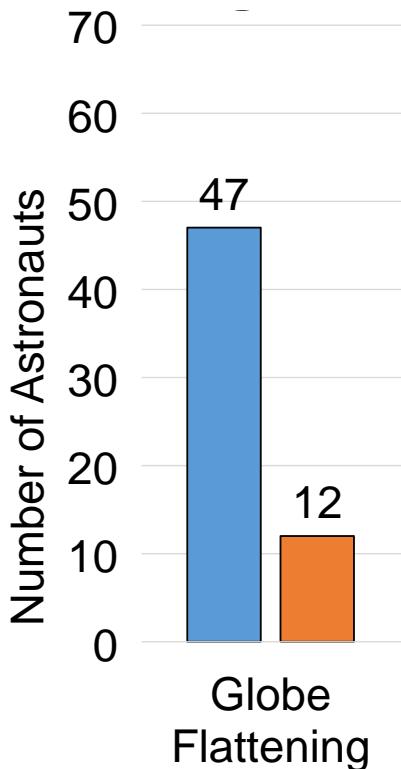


6 days post-flight

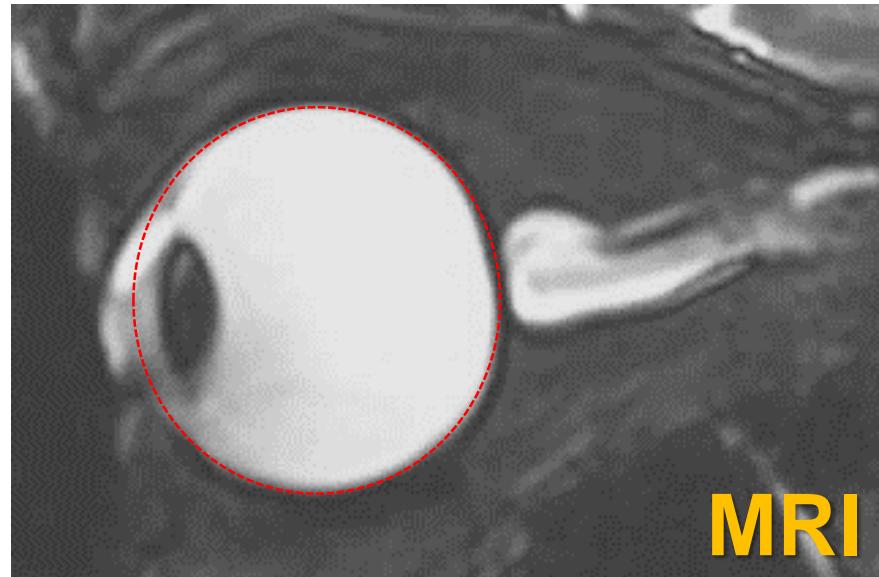
Subjective call from
MRI, ultrasound



Globe Flattening



Terrestrially: Globe flattening is associated with disc edema resulting from intracranial hypertension.



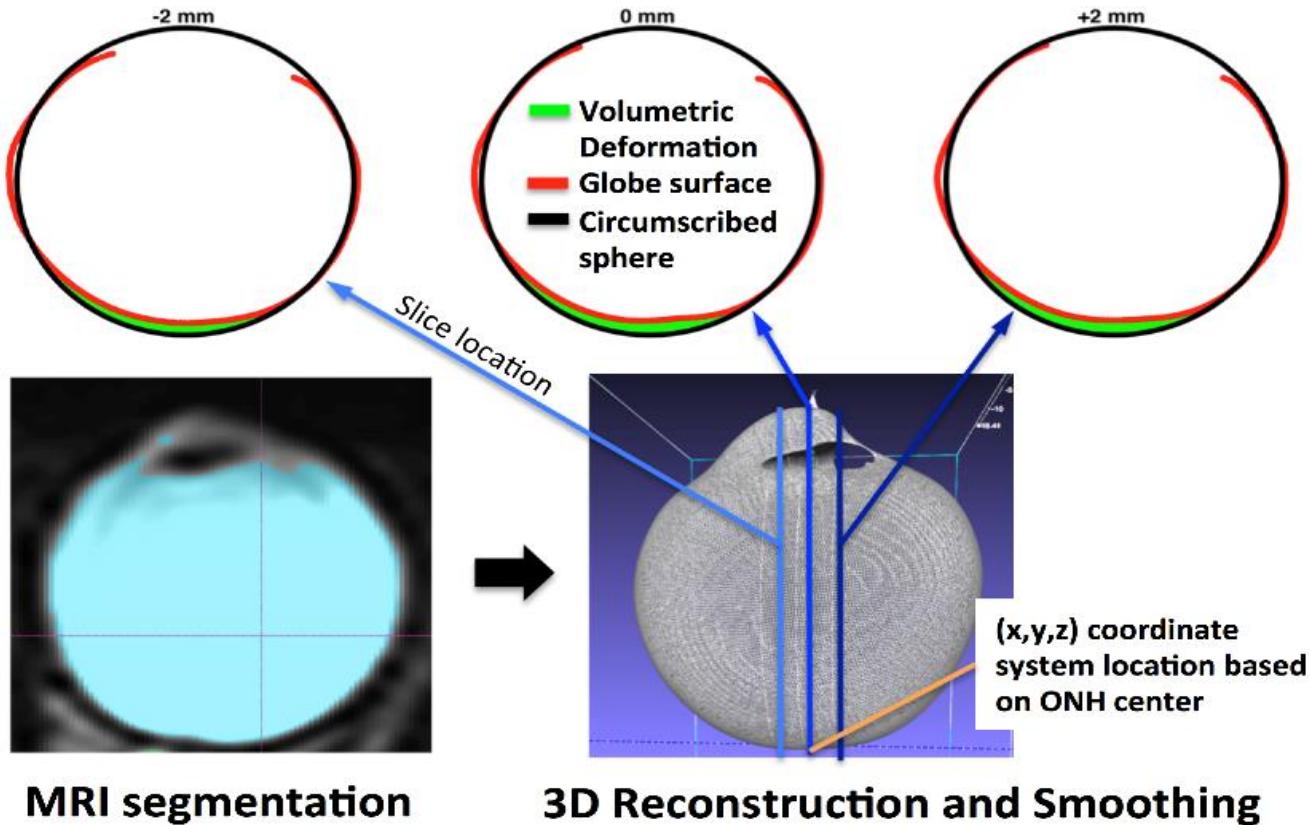
1 year post-flight

Subjective call from
MRI, ultrasound



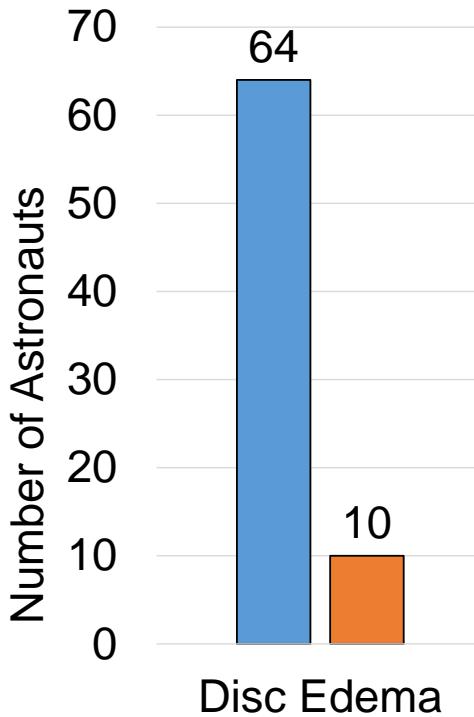
Quantify Globe Flattening

Collaboration with Dr. Bryn Martin, University of Idaho





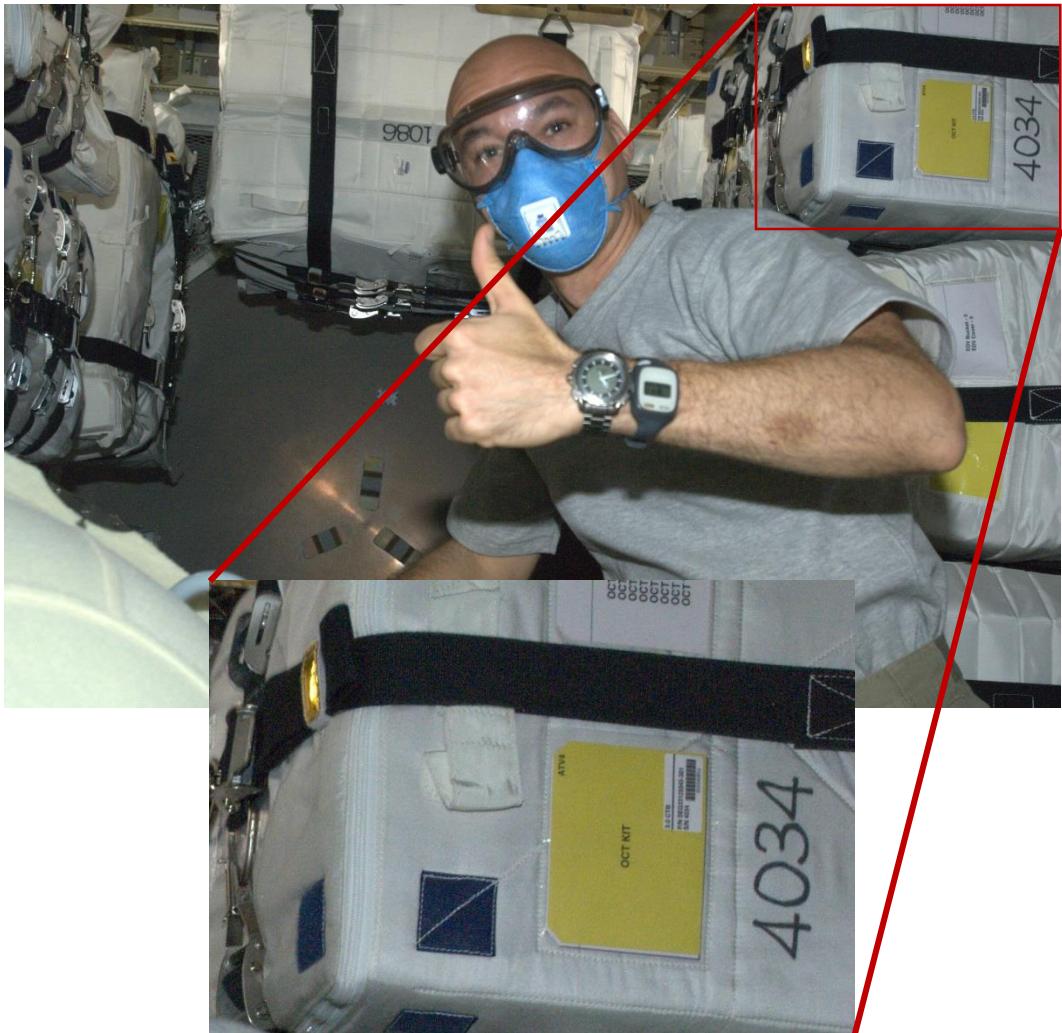
Optic Disc Edema



- Observation of “fuzzy” optic disc on retinal fundus image.
- Score: 0-5
- 64 Pre/Post flight pairs of images
- Observed: Right > Left eye

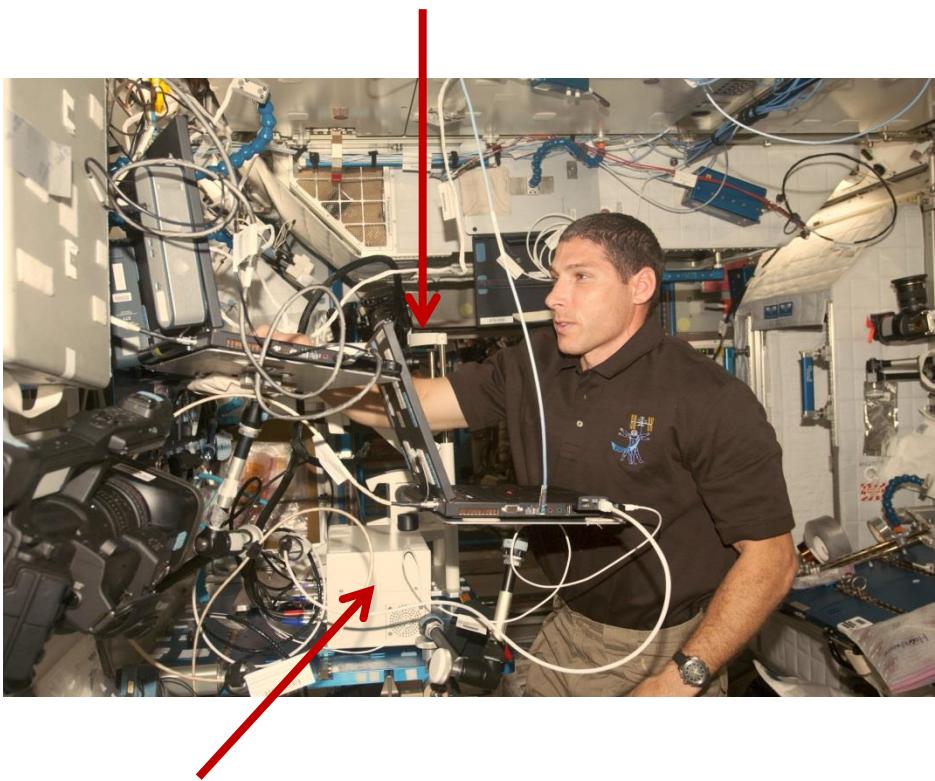


OCT – Journey to the ISS



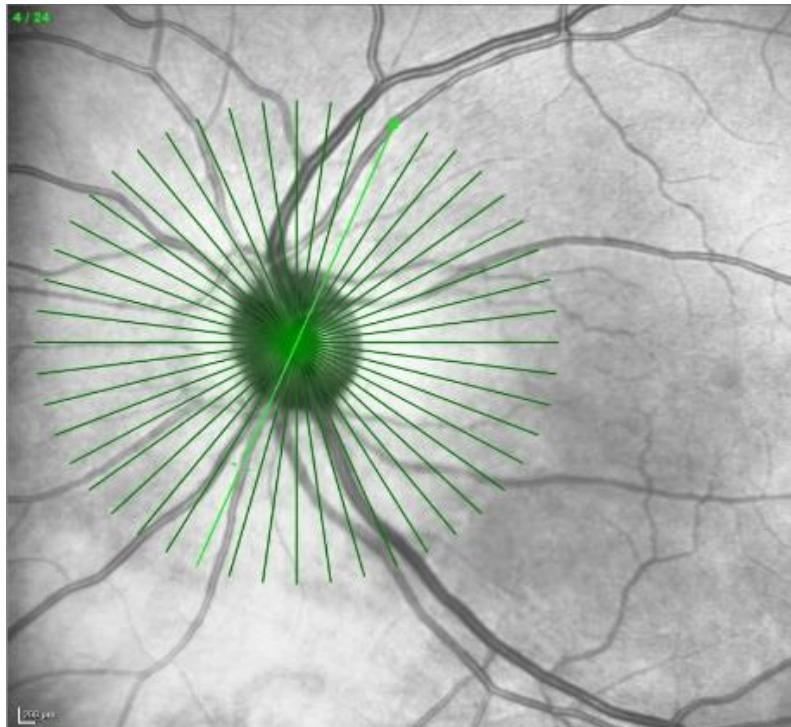


OCT on the ISS

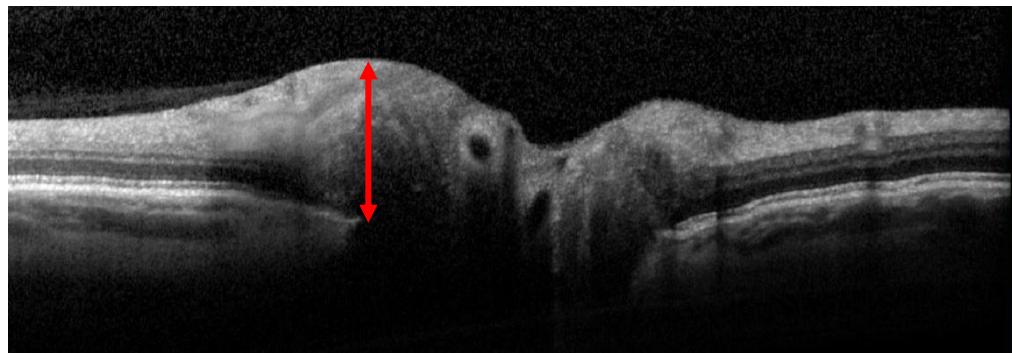
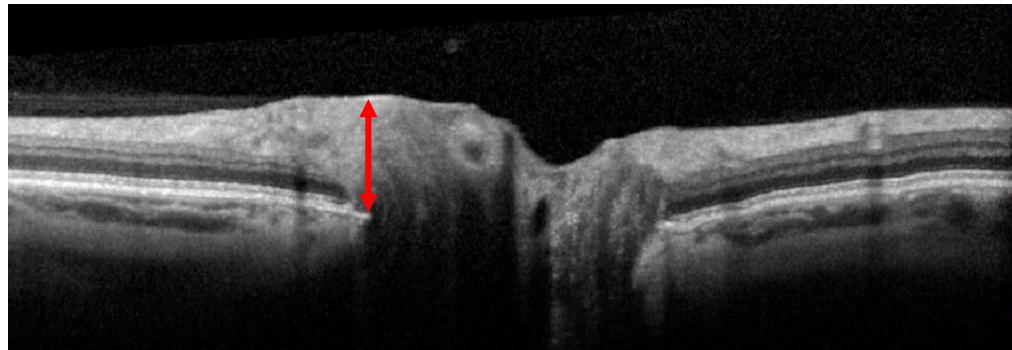




Optical Coherence Tomography



Optic nerve head. Green lines are locations of OCT scans.



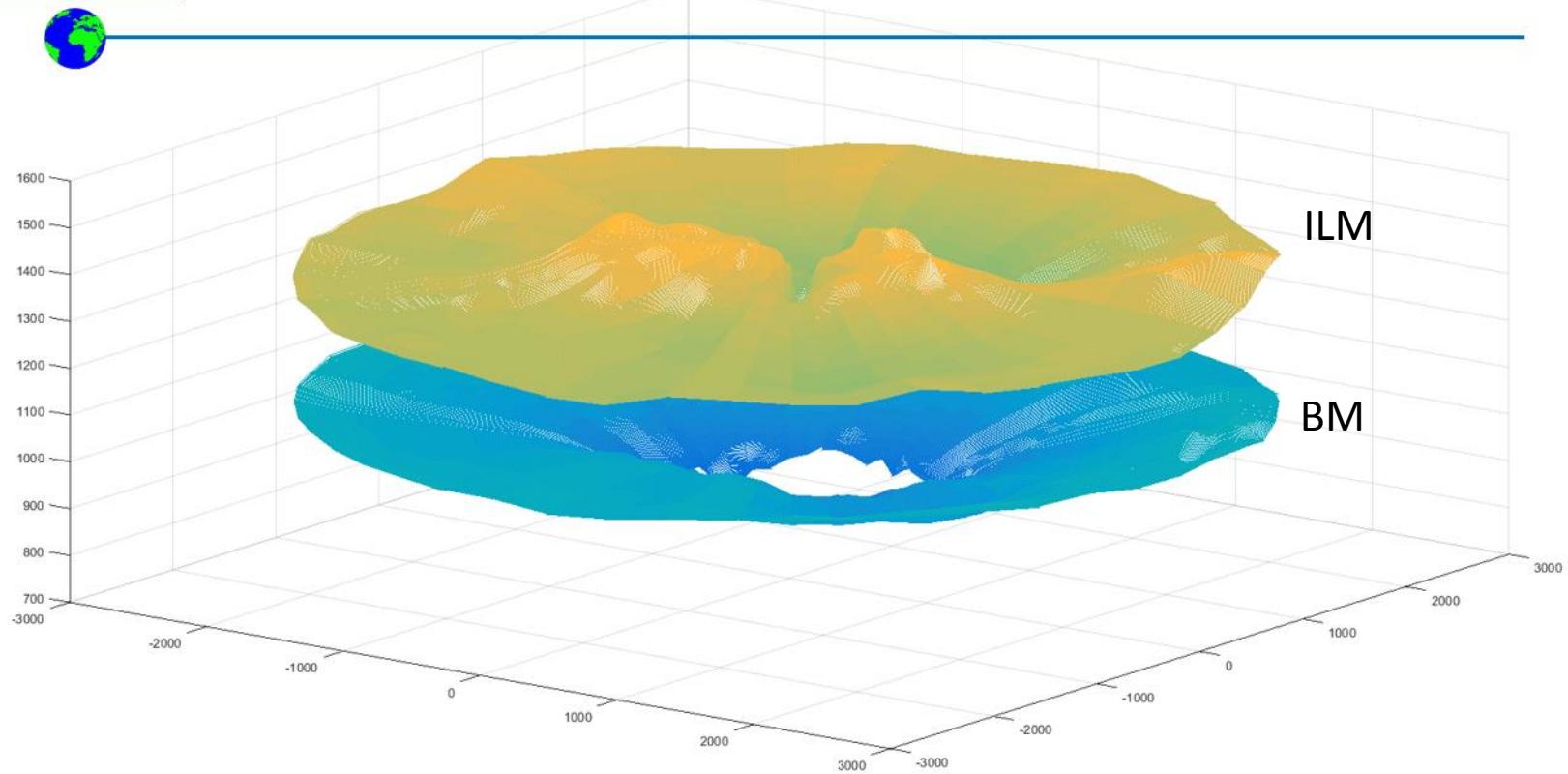
Preflight (top) and postflight (bottom) OCT scans through optic nerve head.

Reconstruct thickness map from 24 OCT images to quantify retinal thickness.



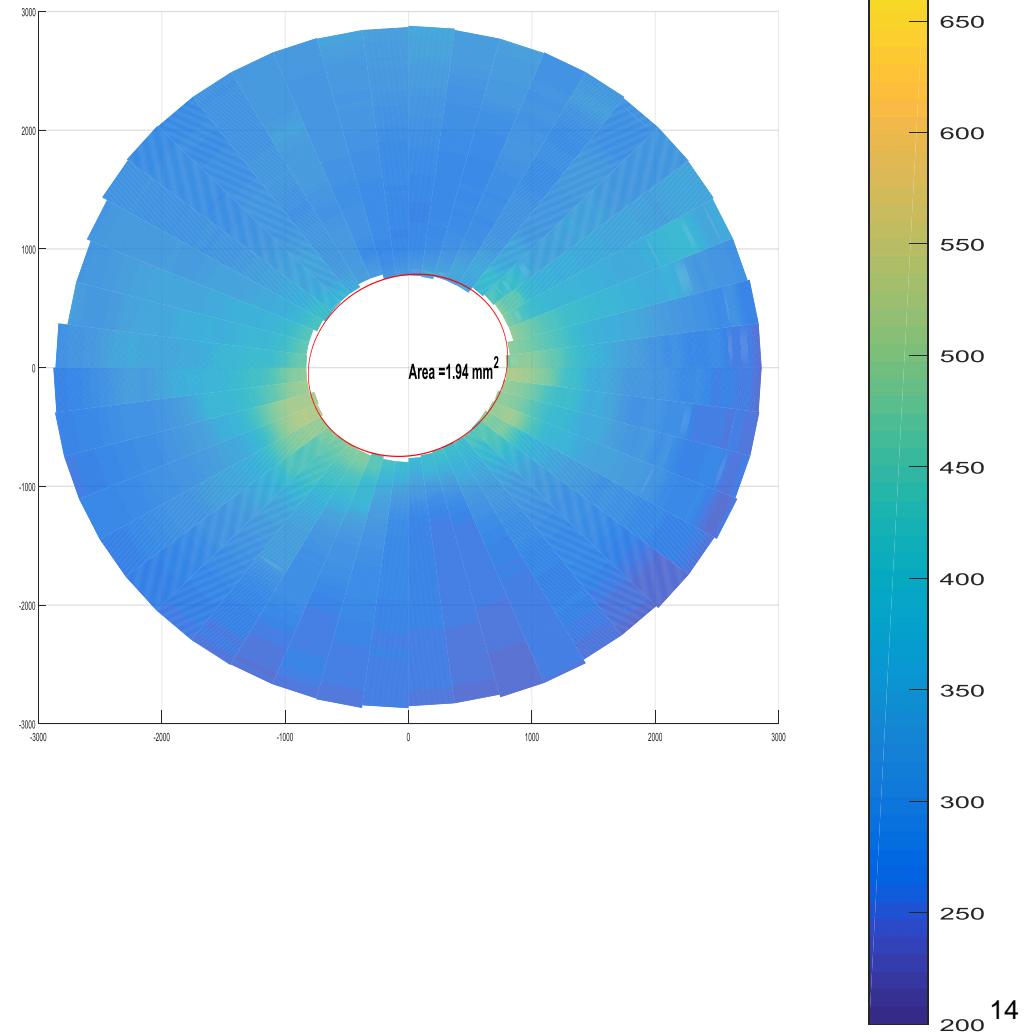
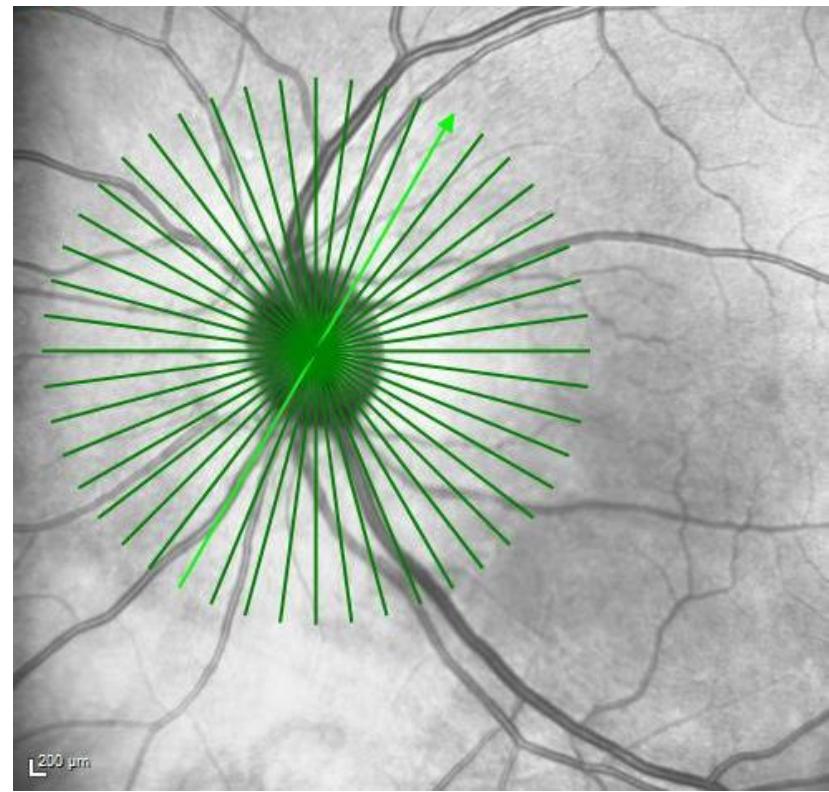
Engorgement of Optic Nerve Head

Preflight FD45 FD150 R-45 R+10 R+45 R+180





ONH Thickness Map





ONH Thickness Map

Preflight



FD45

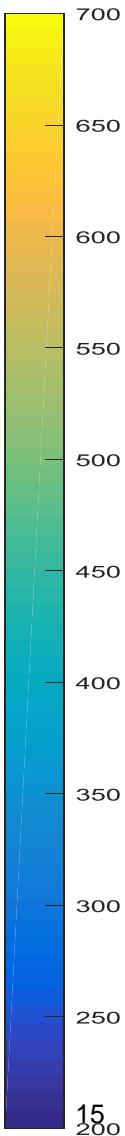
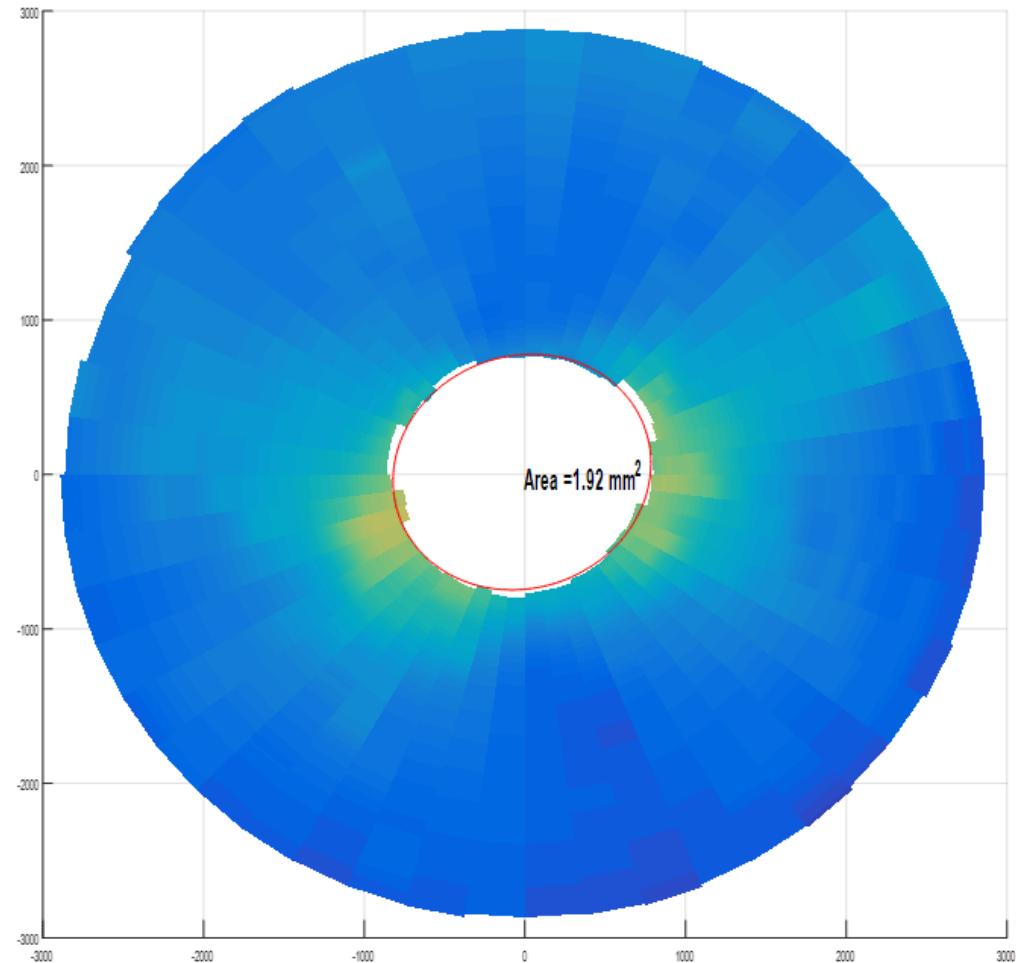
FD150

R-45

R+10

R+45

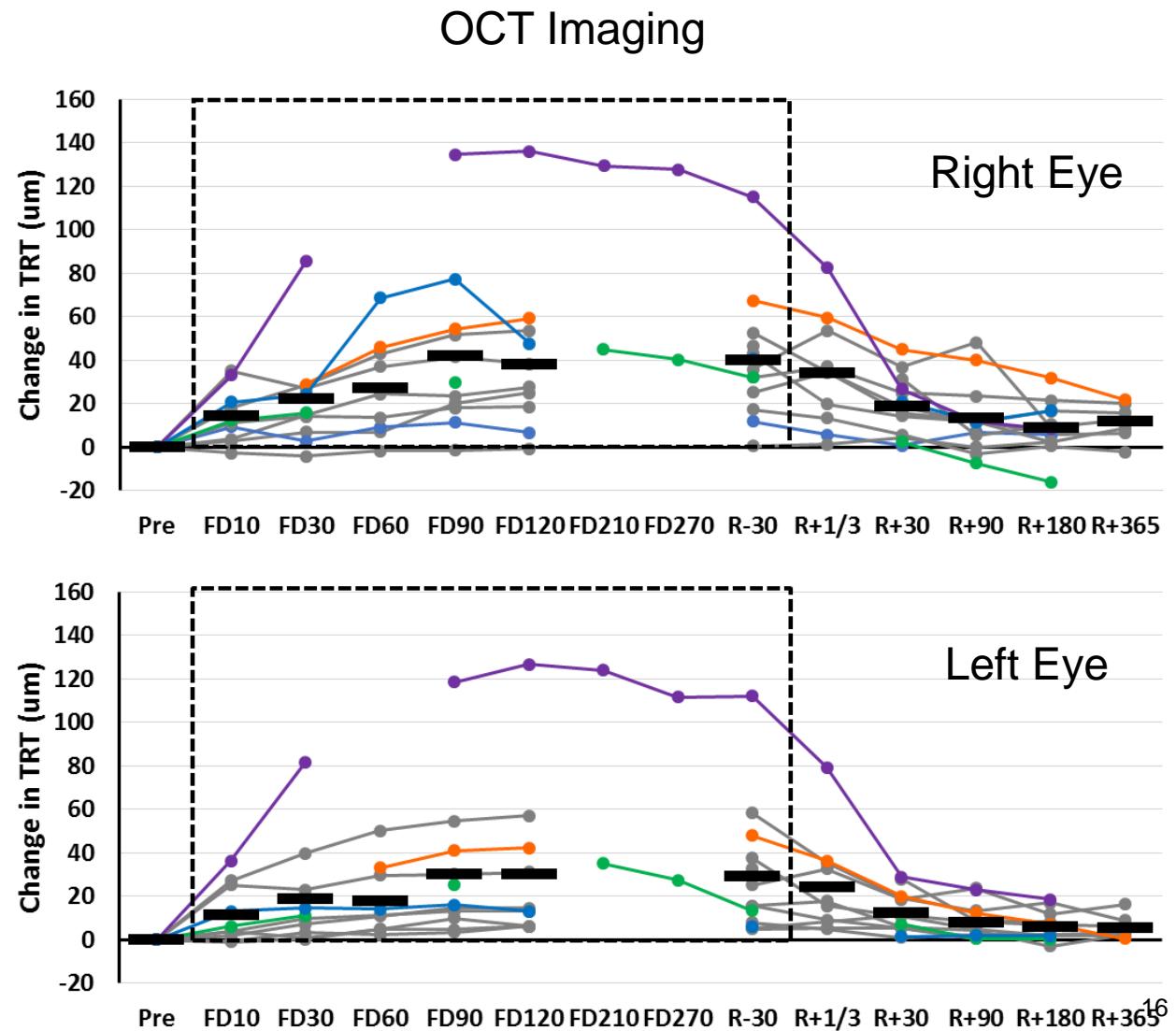
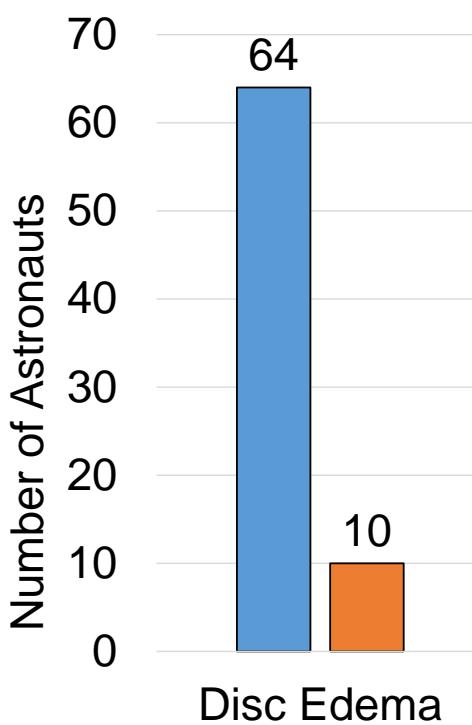
R+180





Fundus Image vs. OCT

Fundus Imaging



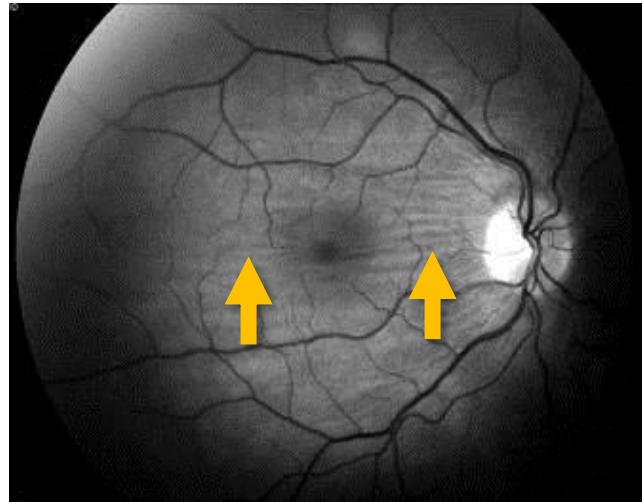
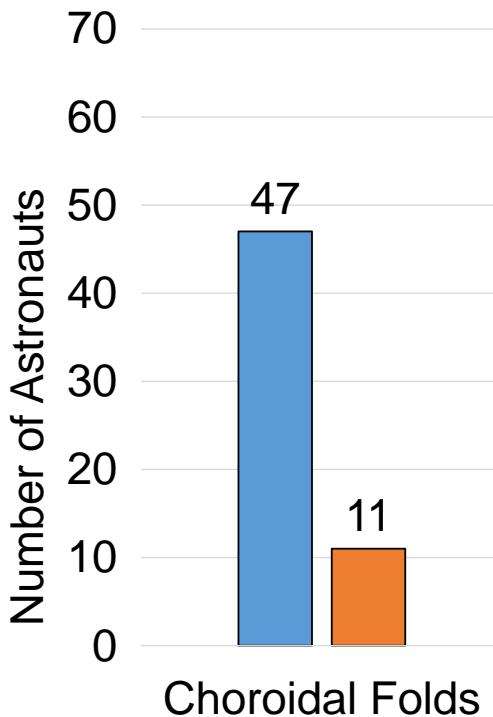


Spaceflight Duration?

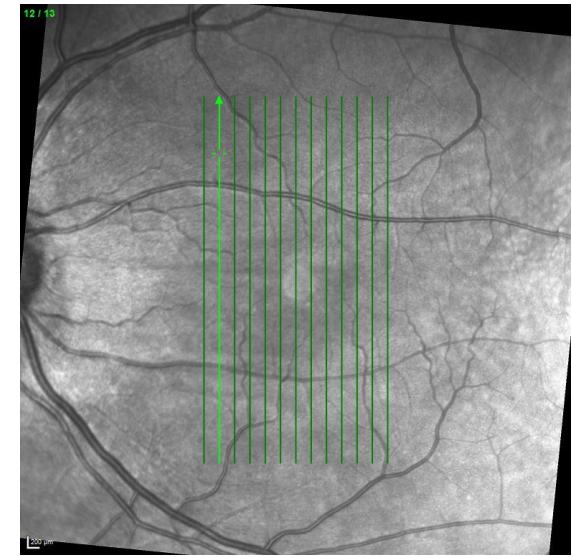
Frisen Grade	Pre-flight	4-6 mo missions			1 year missions		Post-flight
Eye	L-9/6mos	FD30	FD90	FD150	FD270	R-30	R+1/3
Left	0	1	1		1	1	2
Right	0	2	2		2	2	2
Left	0	0	0	0			
Right	0	0	0	0			



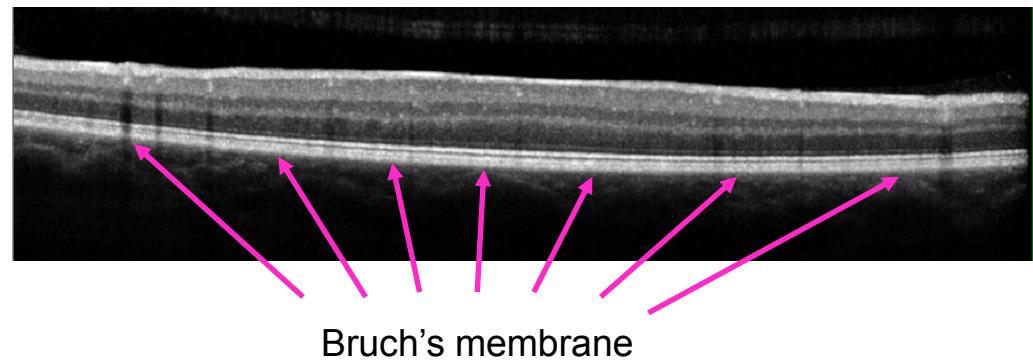
Choroidal Folds



Fundus Image



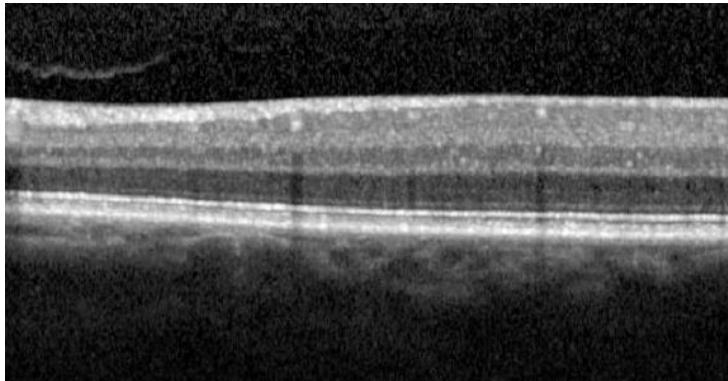
IR Image (OCT Camera)



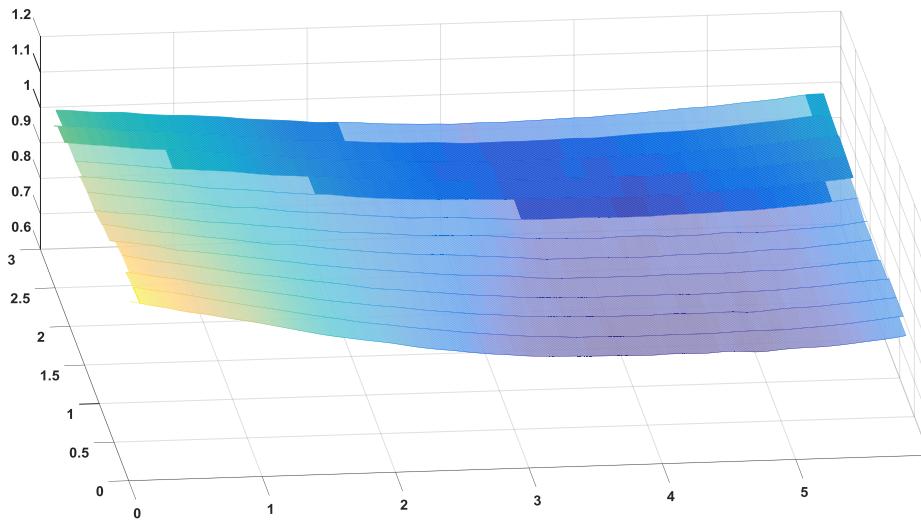
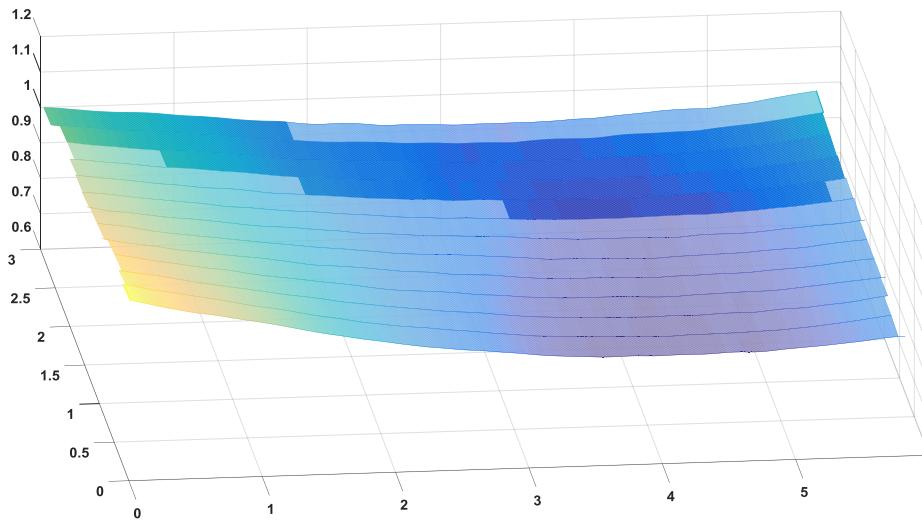
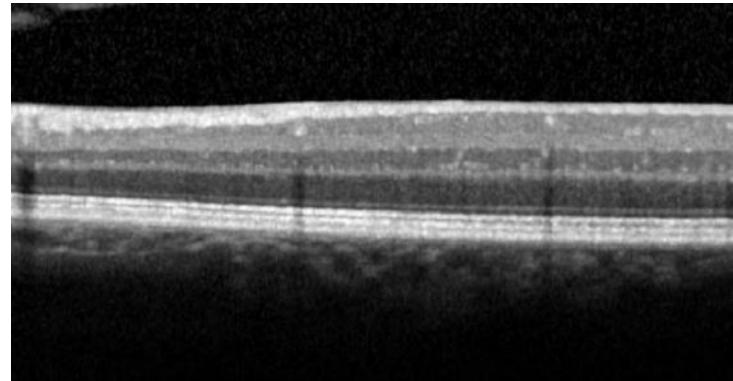


No Choroidal Folds

Pre-flight: Seated



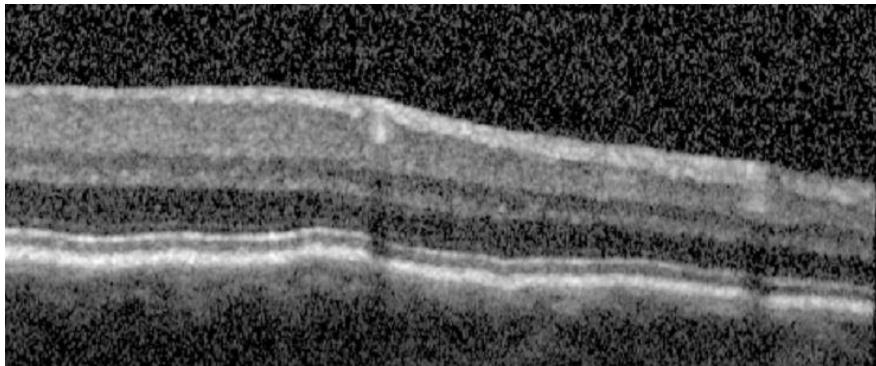
FD150



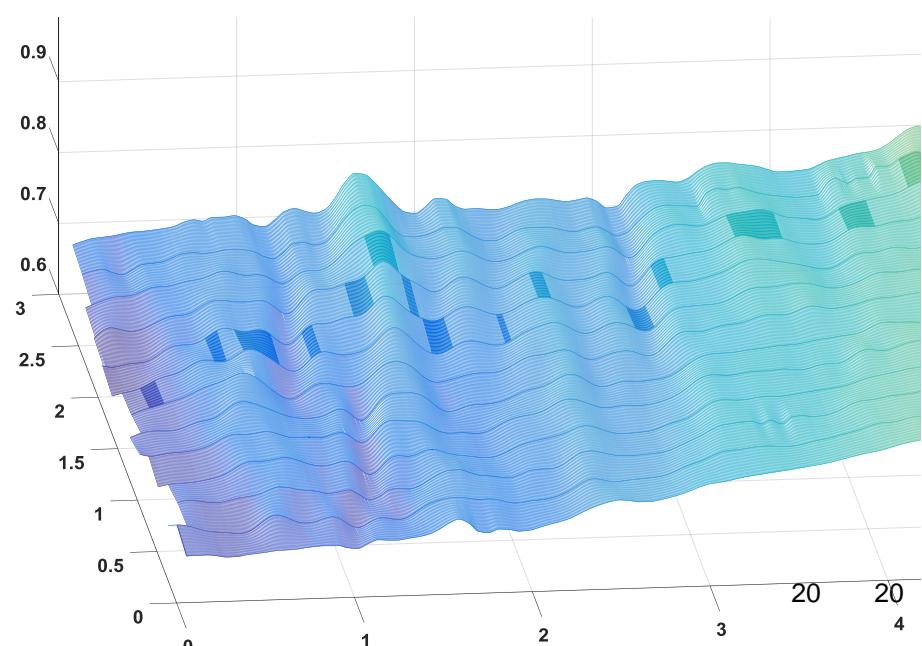
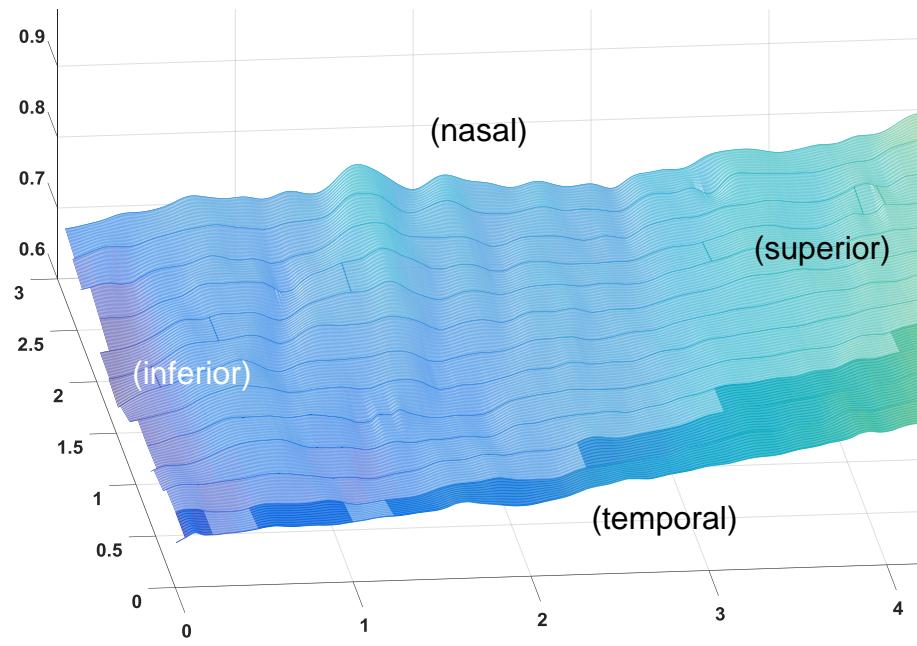
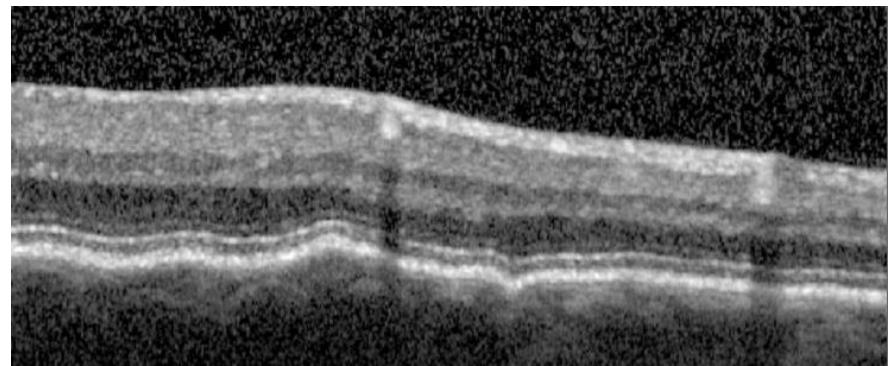


Choroidal Folds

Pre-flight: Seated

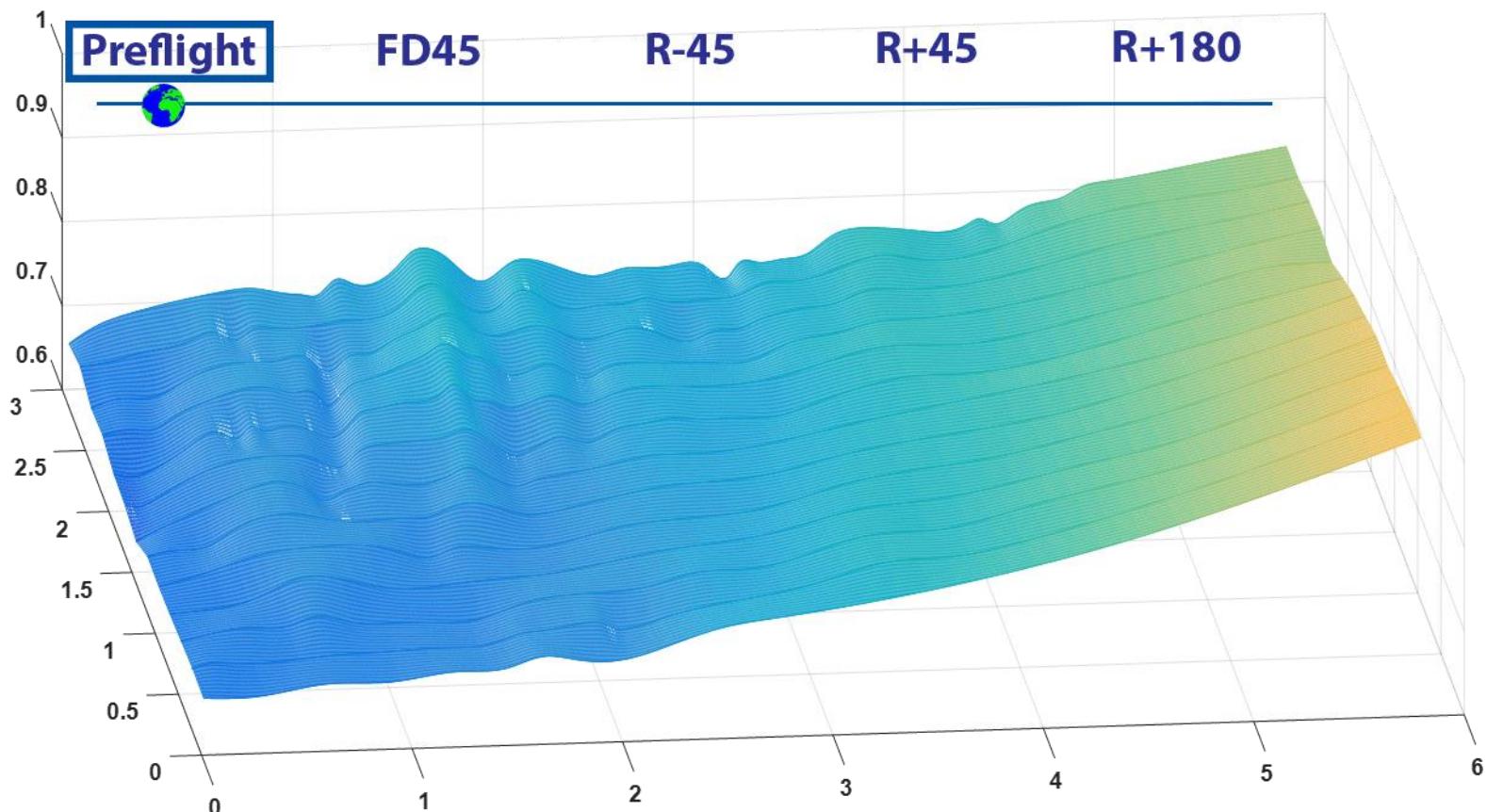


FD150



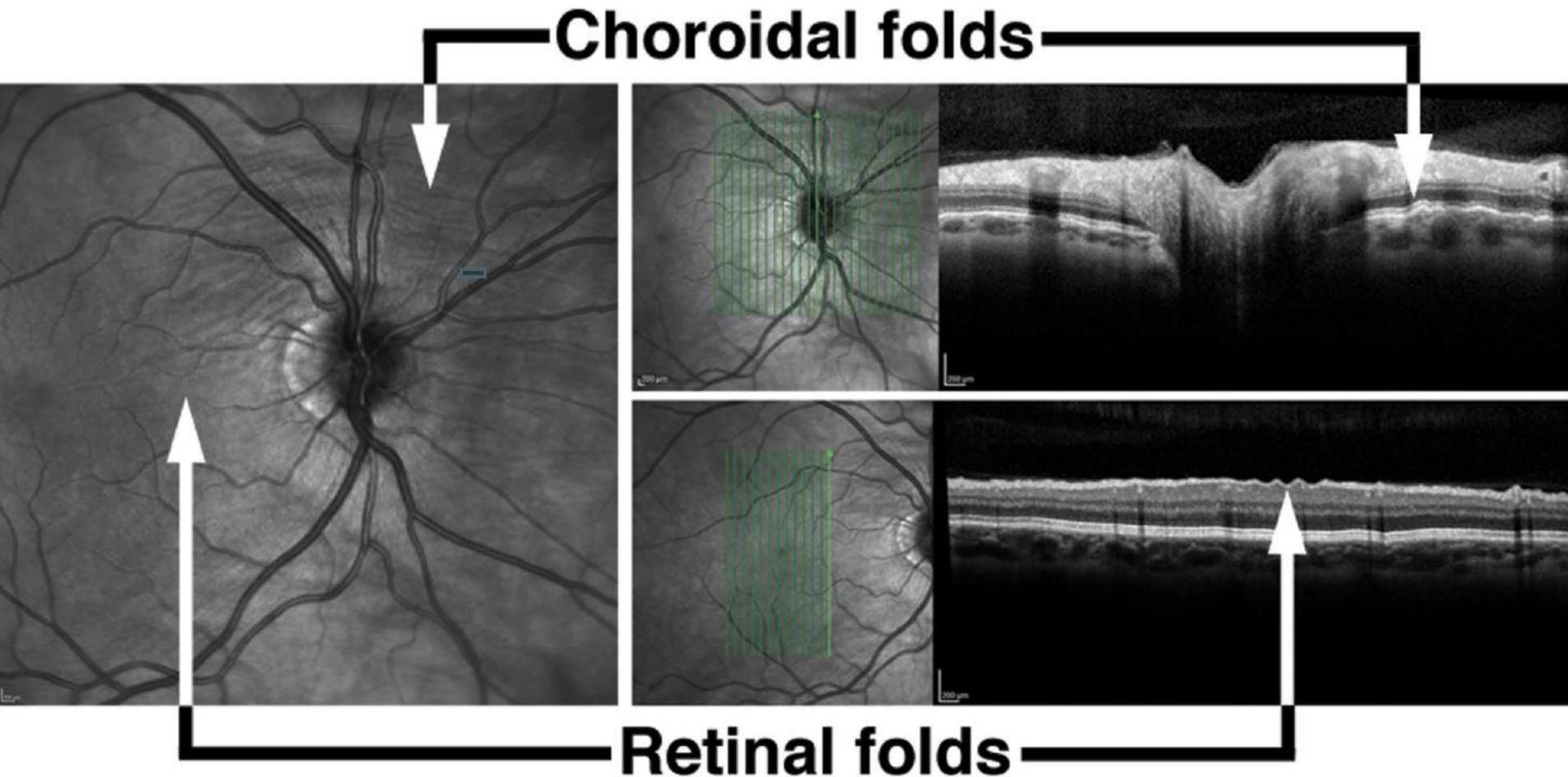


Choroidal Fold Progression



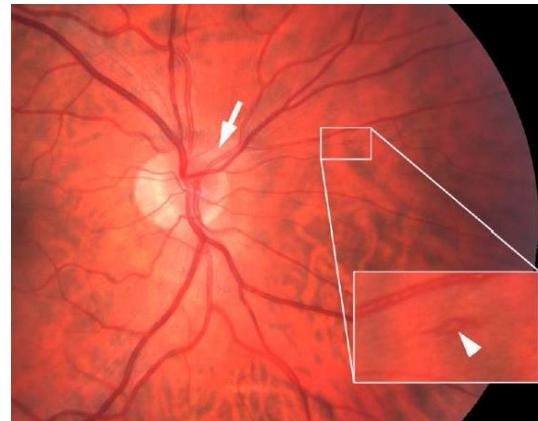
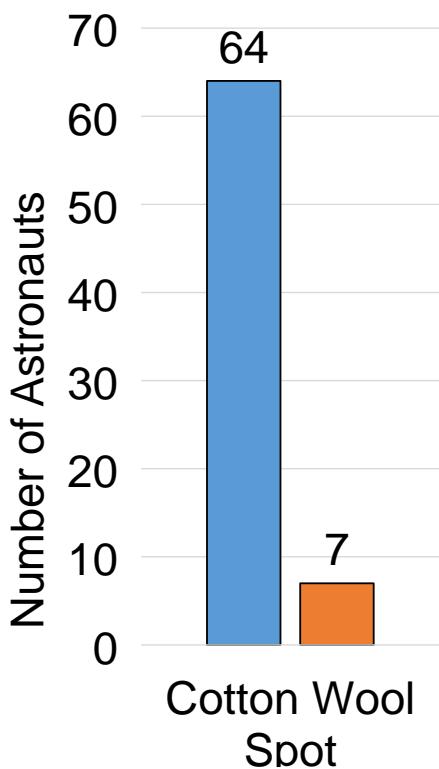


Choroidal/Retinal Folds

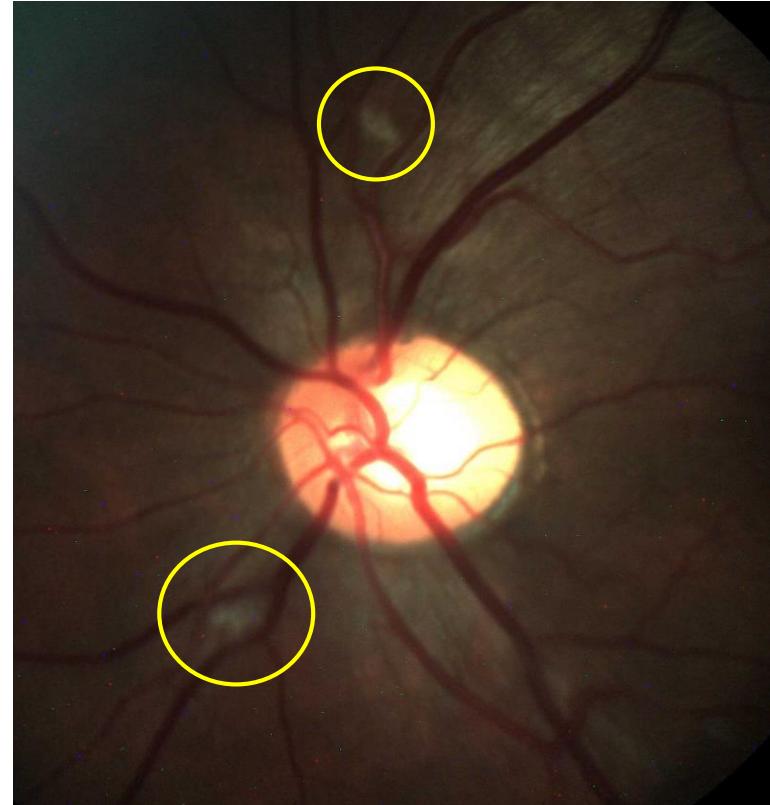




Cotton Wool Spot



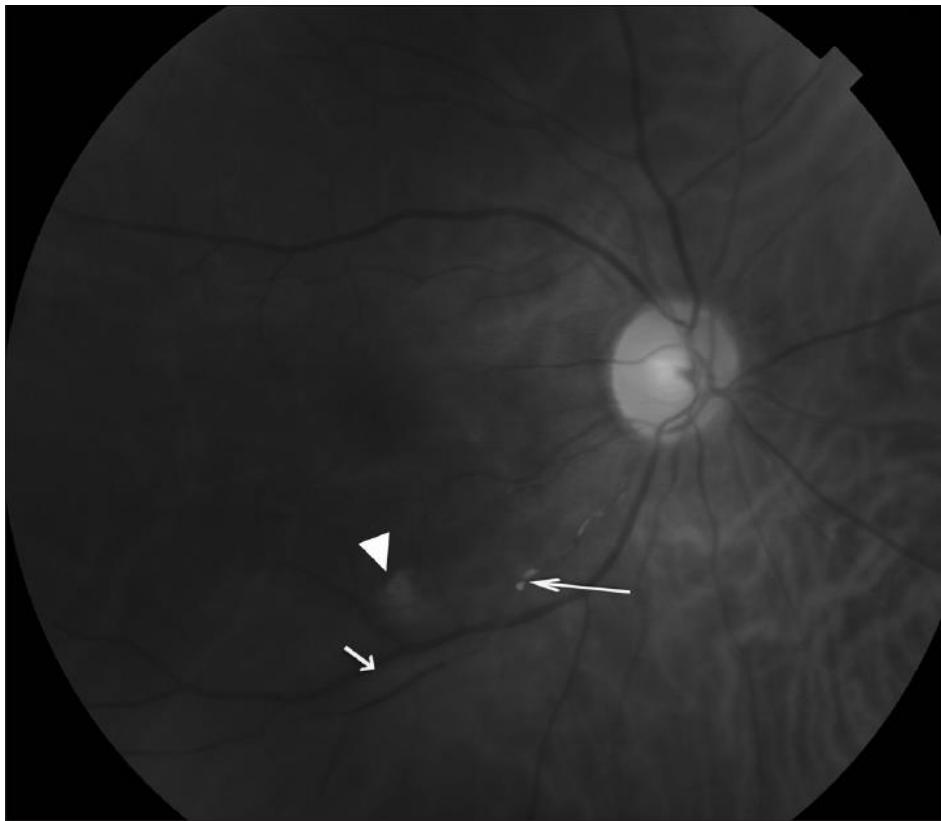
Mader et al., J Neuro-Ophthalmol, 2016



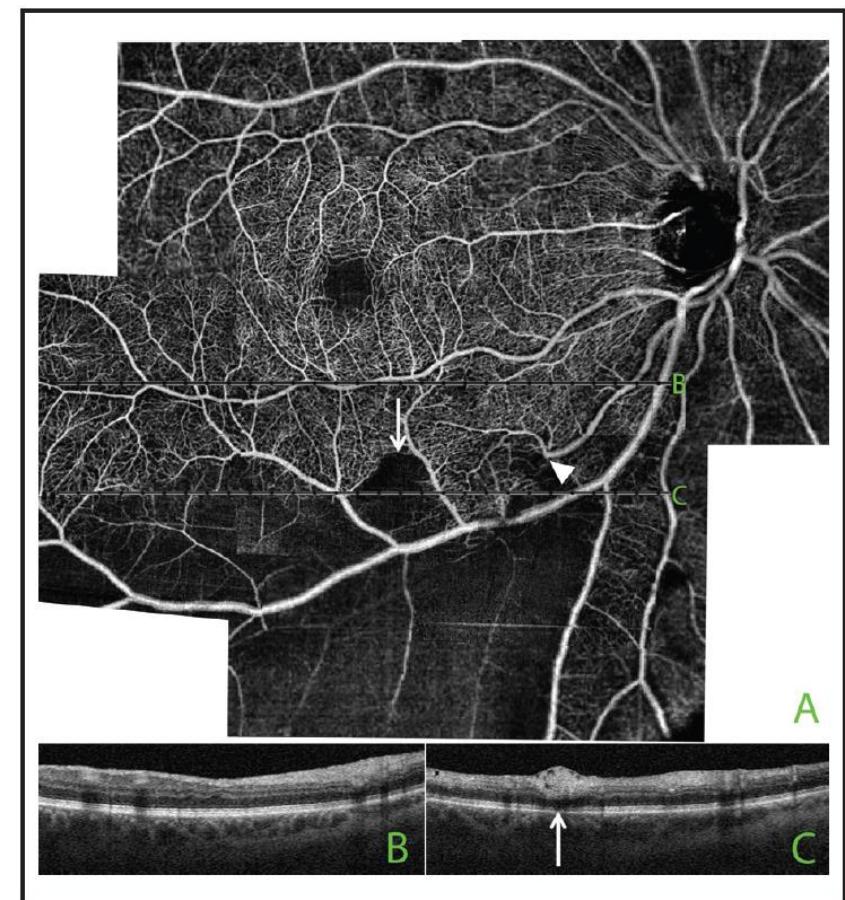


OCT Angiography

Fundus Photograph



OCT Angiography



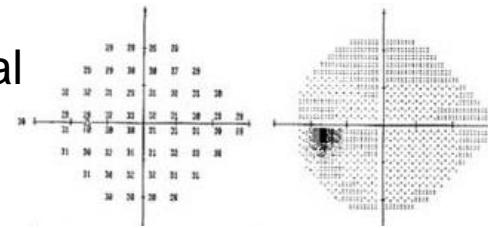


Visual Function (Threshold Visual Fields)

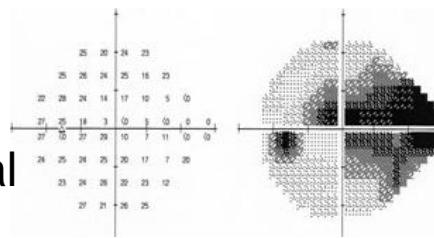
Humphrey Automated Perimetry



Normal



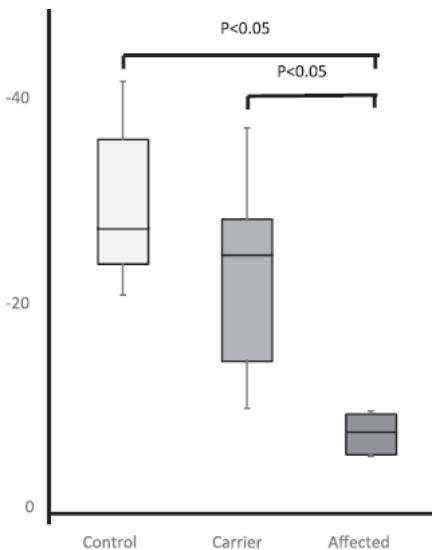
Abnormal



Potential Compact Visual Fields Device for ISS

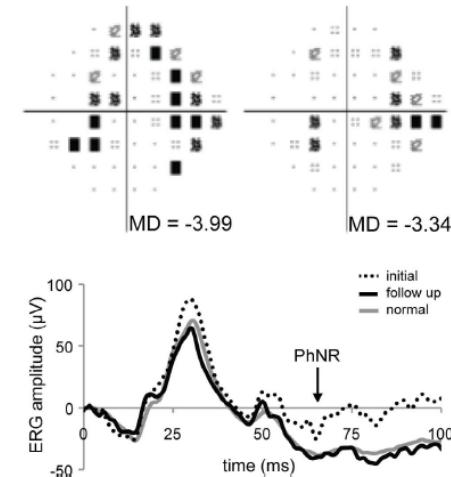
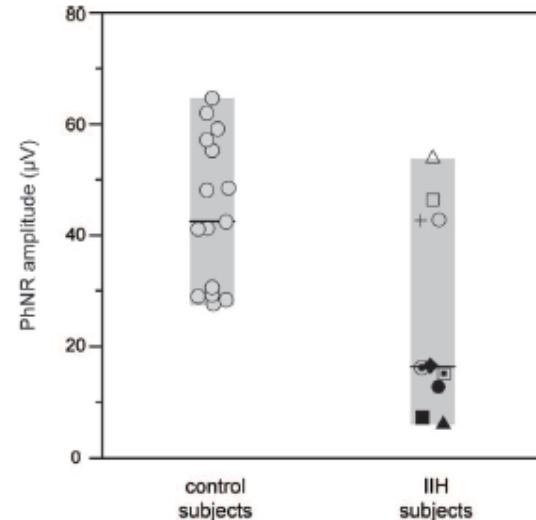


ERG – Slide here



ERG can detect significant deficits in Retinal Ganglion Cell Function in population of mitochondrial DNA mutations (some may be associated with 1C pathway)

Karanjia R et al 2017

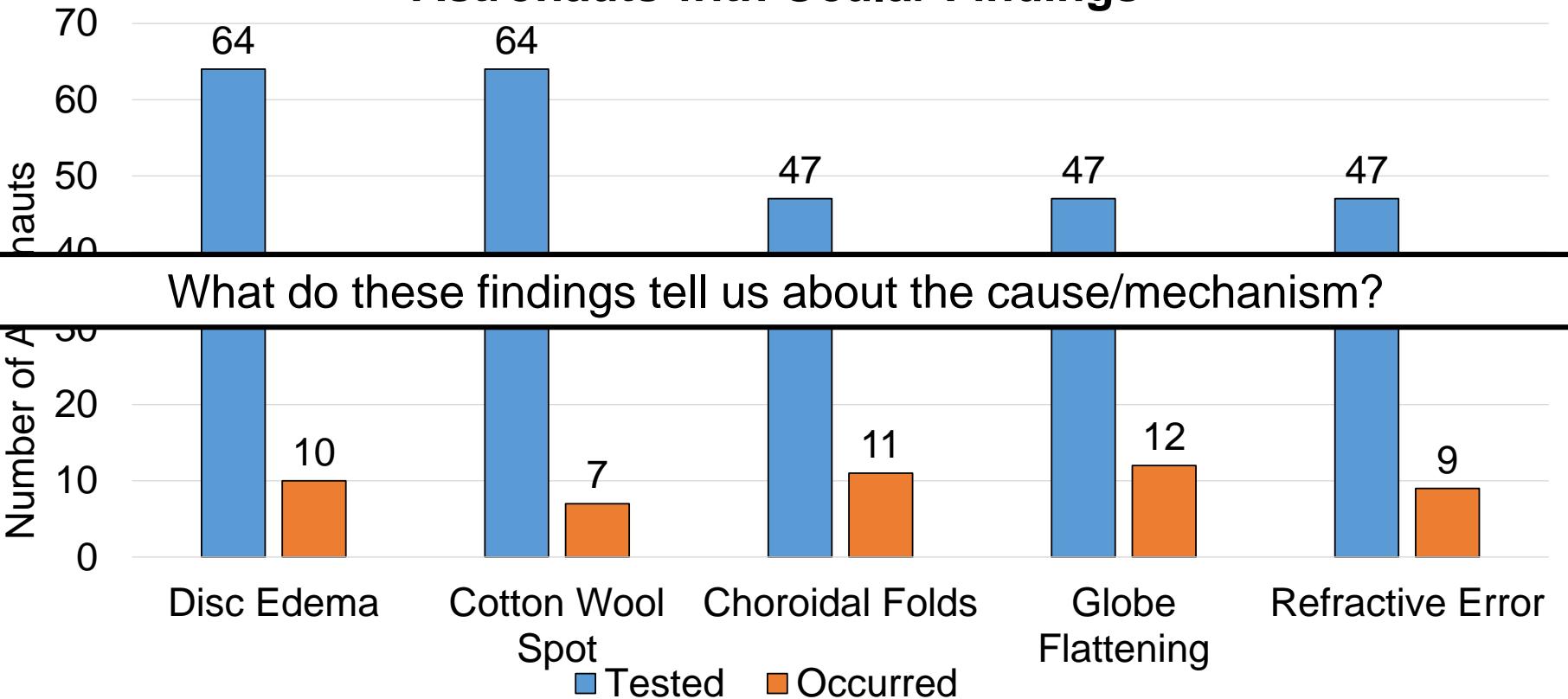


Moss H et al 2015



Ocular Findings through 2016*

Astronauts with Ocular Findings



*USOS astronauts only 27

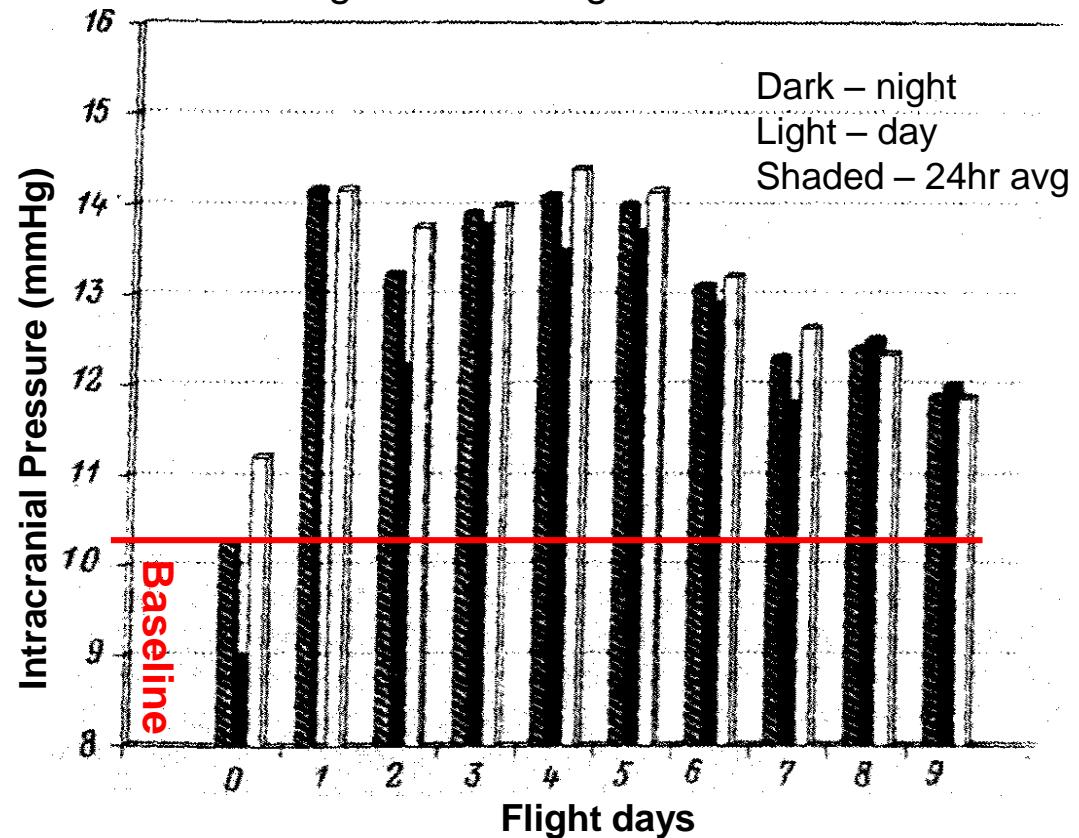


ICP during Space Flight

- ICP has never been measured in humans during spaceflight
 - Russians measured ICP invasively in a Macaque monkey in 1992, during a 10-day Bion satellite flight, with an intracranial (epidural) probe
 - ICP increased as high as 30% compared with preflight measurements
 - CO₂ did not exceed 1mmHg, ISS mission average=3.56mmHg



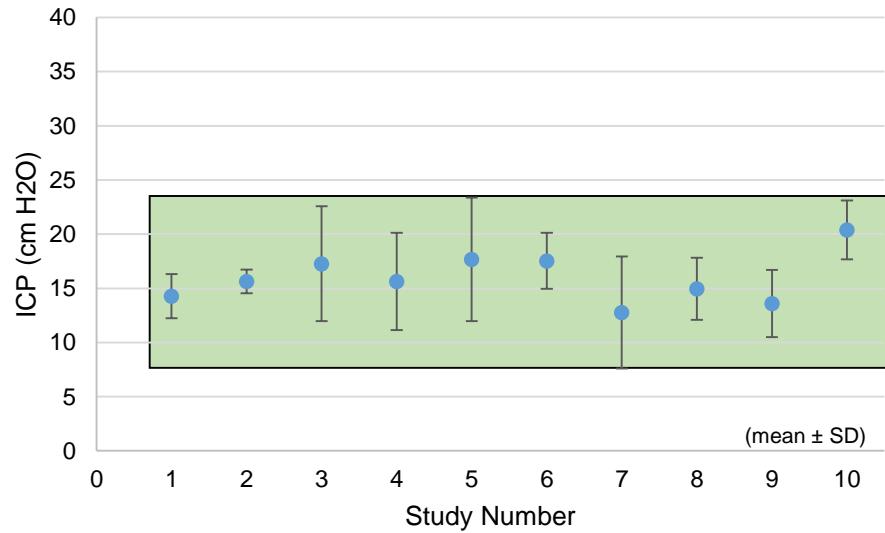
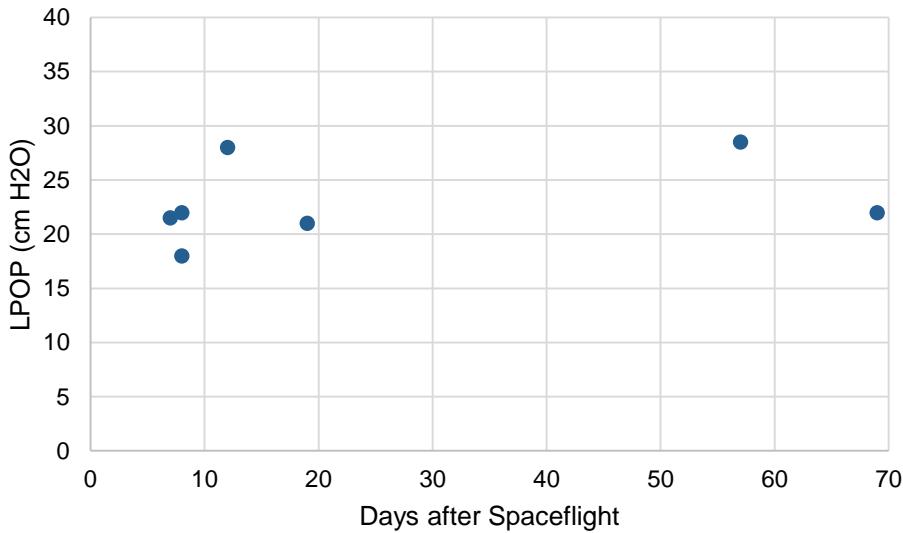
Trambovetskiⁱⁱ et al. 1995. Intracranial pressure in monkeys during the flight of Cosmos-2229. [Aviakosm Ekolog Med.](#)





Intracranial Pressure

Idiopathic Intracranial Hypertension patients: optic disc edema and globe flattening



ICP after spaceflight may not be pathologically elevated.

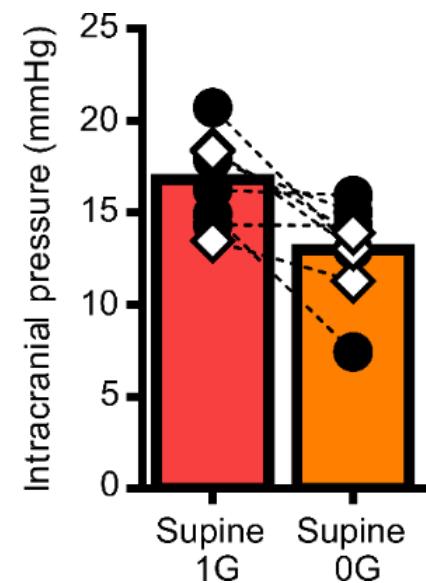
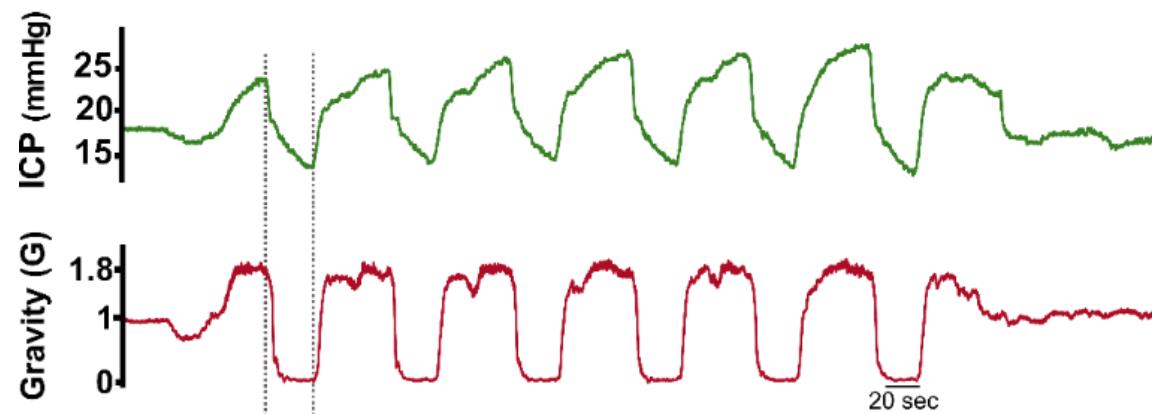
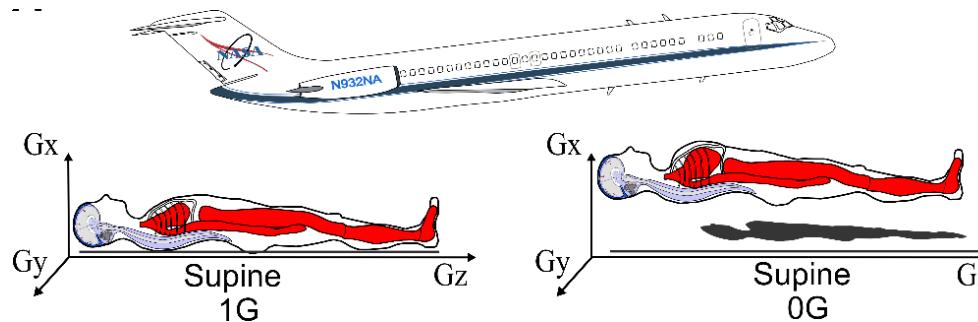
What was ICP during spaceflight?

*USOS crew only

Publication	Postion	n
Eklund, Ann Neurol, (2016) 80:269-276	Supine	11
	Supine	11
Berdahl, IOVS, (2008) 49:5412-18	Supine	68
	Supine	39
Berdahl, Ophthalmology, (2008) 115:763-68	Supine	49
Ren, Ophthalmology, (2010) 117:259-66	Supine	71
Petersen, AJPR, (2015) 310:R100-4	Supine	9
Qvarlander, JAP, (2013) 115:1474-80	Supine	27
Edsbagge, AJPR, (2004) 287:R1450-5	Supine	34
Lawley, J Physiol, (2017) 15(595):2115-2127	Supine	8



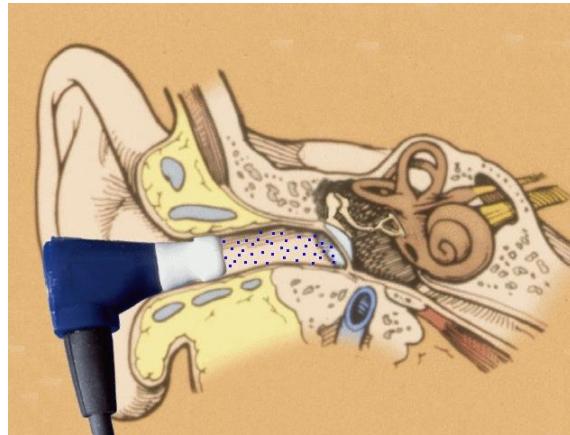
Direct ICP Measures



Lawley JS et al 2017

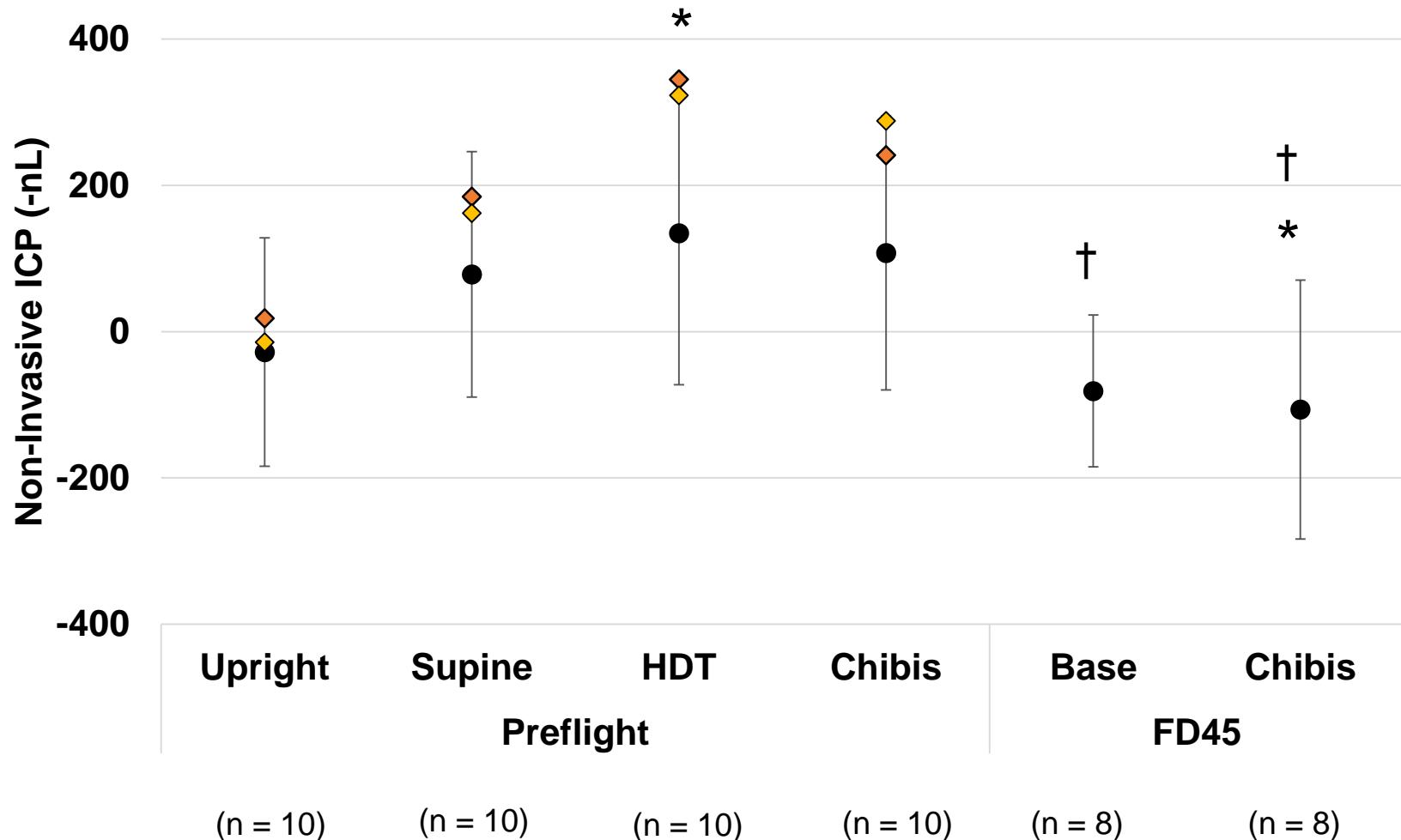


CCFP & DPOAE





Tympanic Membrane Displacement: CCFP



(mean \pm standard deviation)

* p < .05 vs. Upright

† p < .05 vs. Supine



Name change: SANS

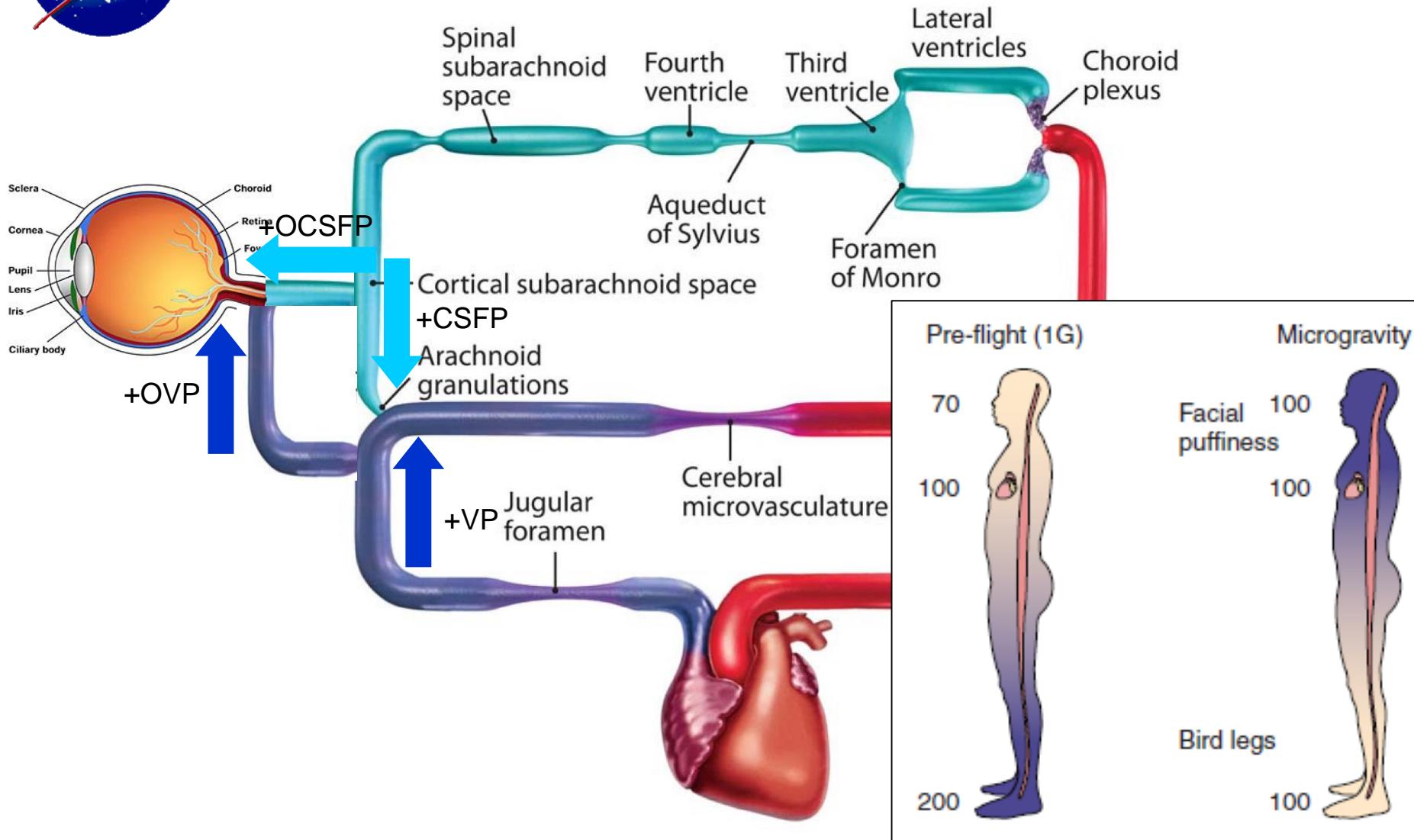
"I only have 2 concerns with the name VIIP. Crew members do not have "Vision Impairment" and it doesn't appear that "Intracranial Pressure" is pathologically elevated."

*- Dr. Bill Tarver, Flight Surgeon
NASA Human Systems Risk Board Presentation*

Spaceflight Associated Neuro-ocular Syndrome
(SANS)

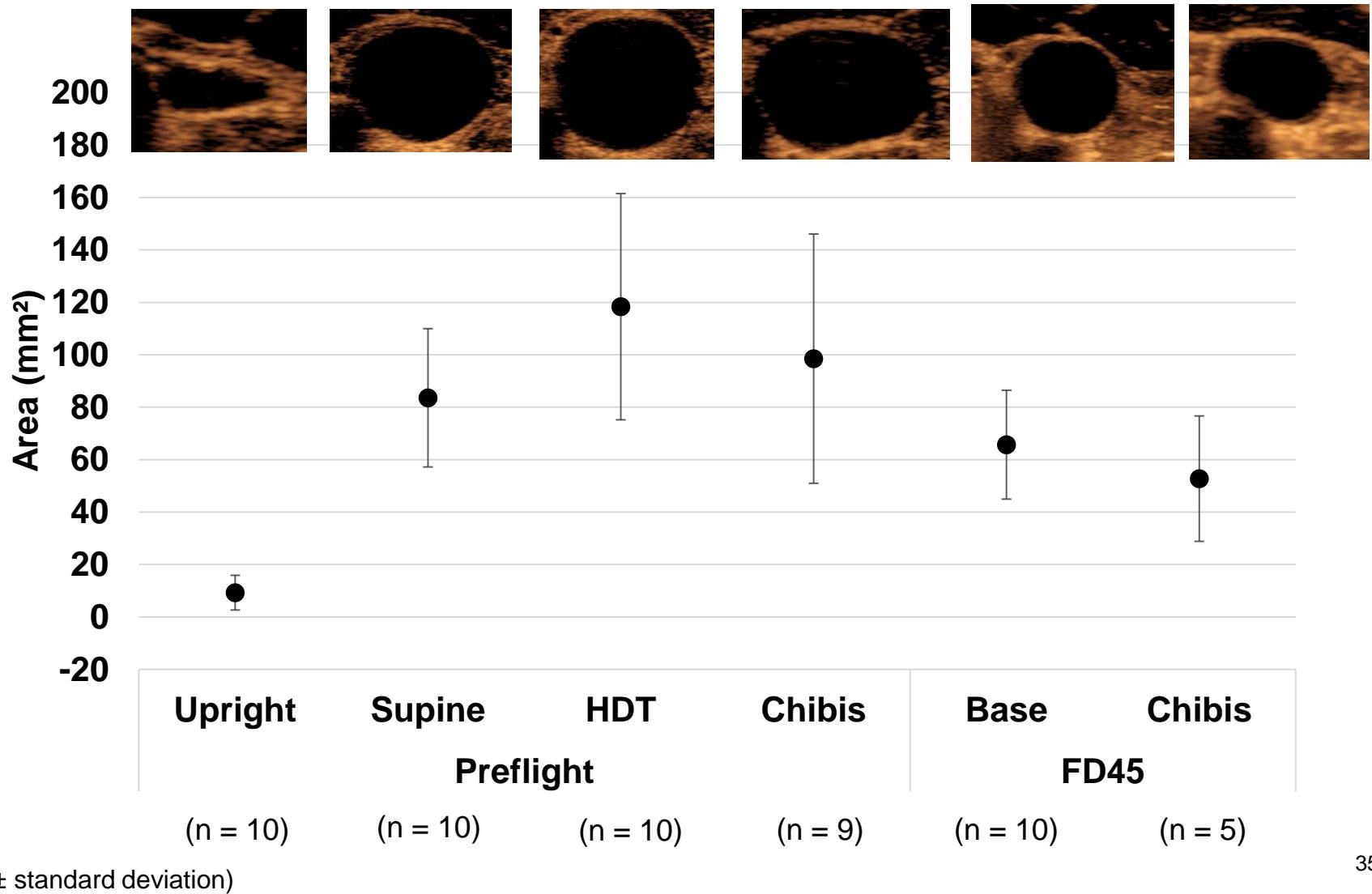


Fluid Shifts



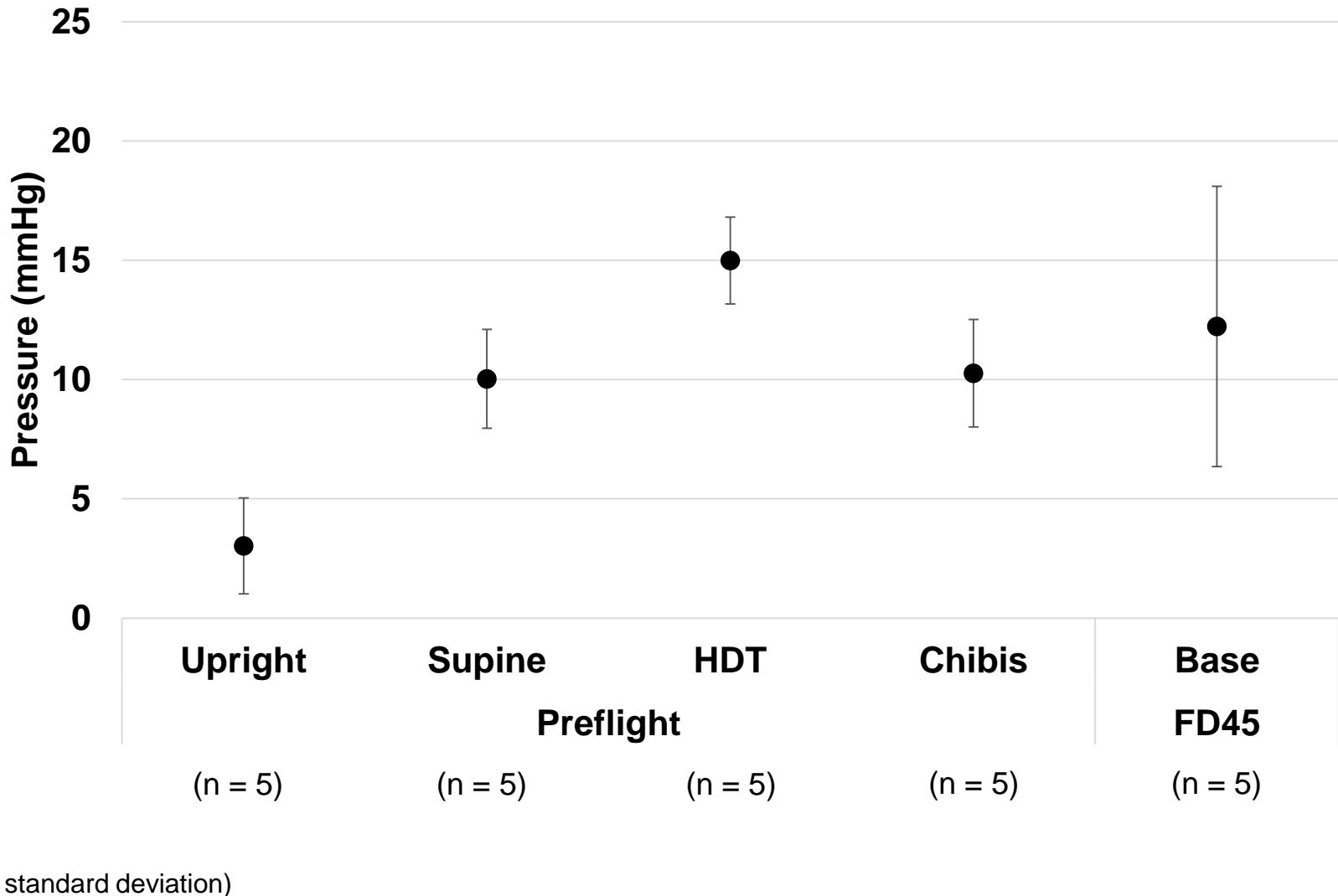


Internal Jugular Vein Area



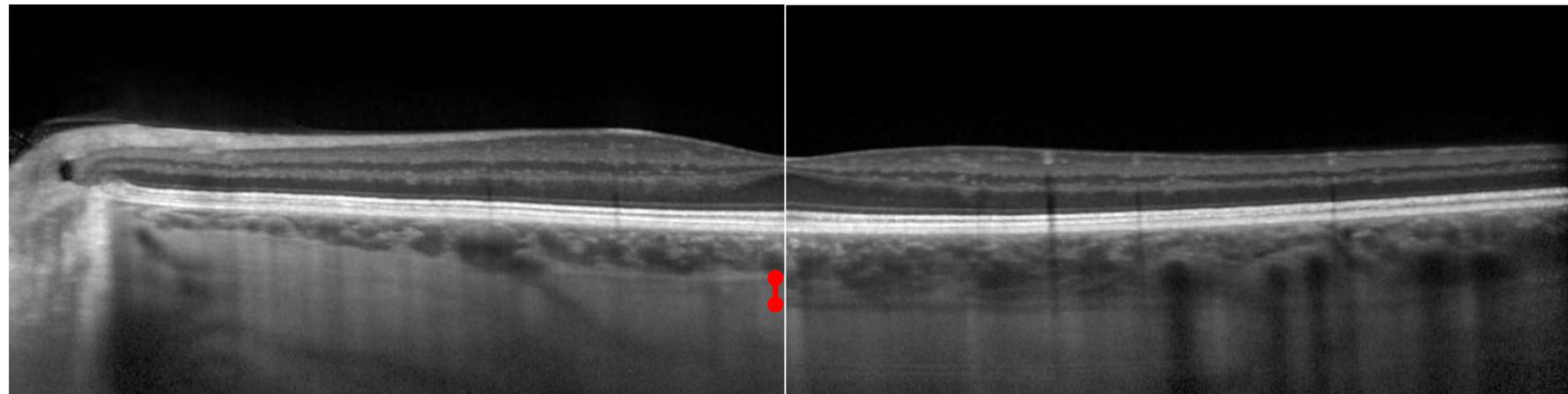
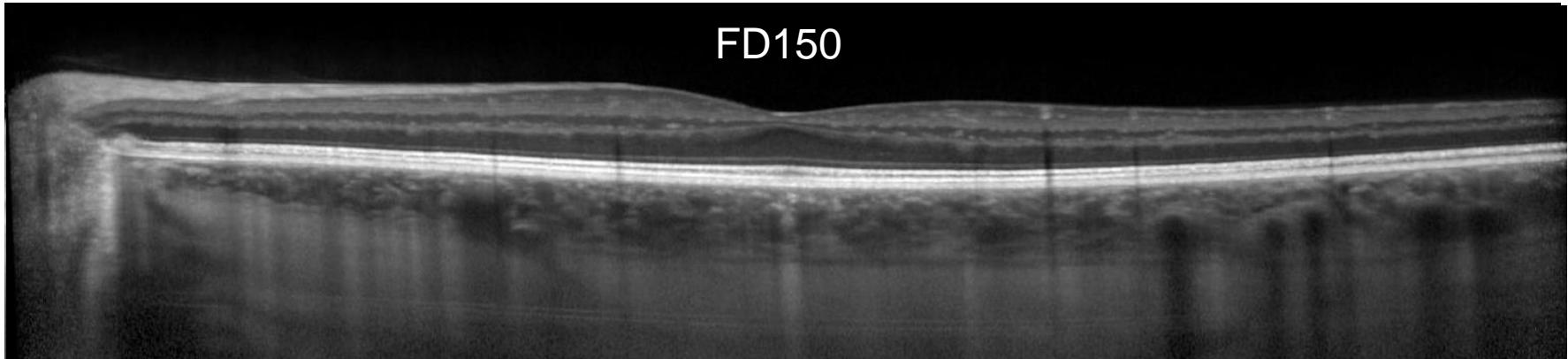


Internal Jugular Vein Pressure





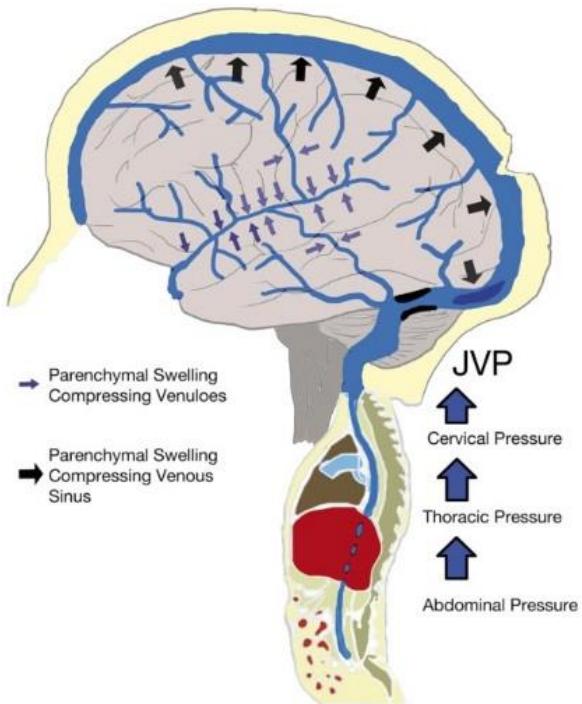
Fluid Shifts in the Eye





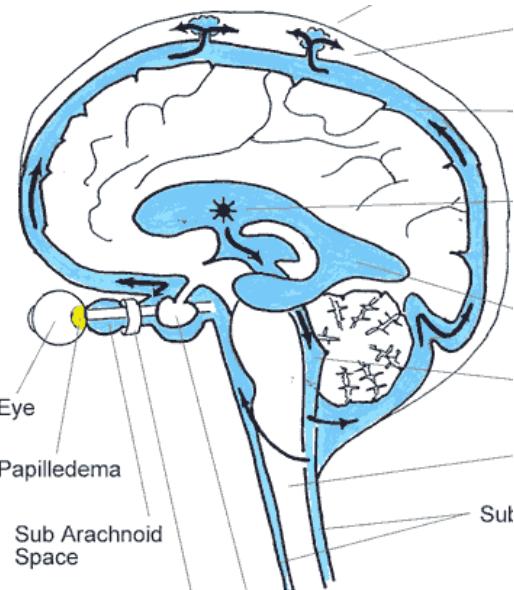
Fluid Shifts

Venous Outflow Restriction

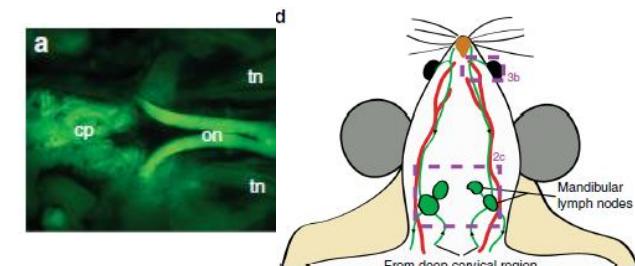


Wilson MH 2016

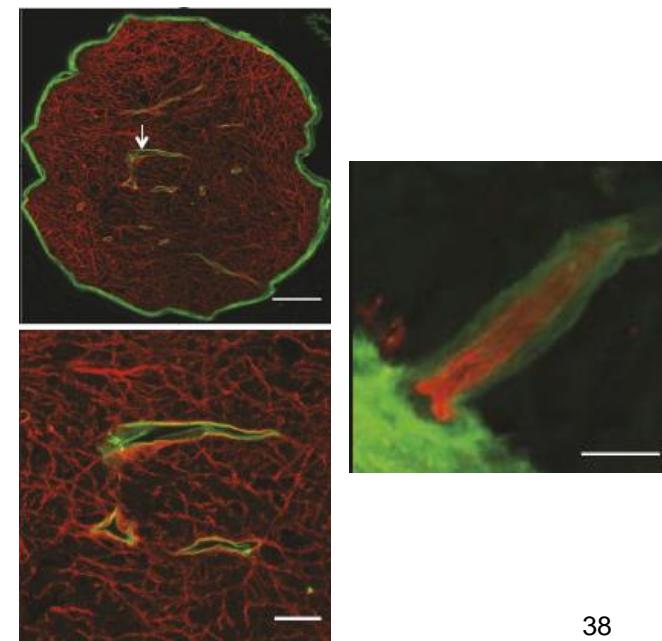
Cerebrospinal Fluid (CSF) Glymphatics & Lymphatics



Kumar KN et al 2012



Ma Q et al 2017

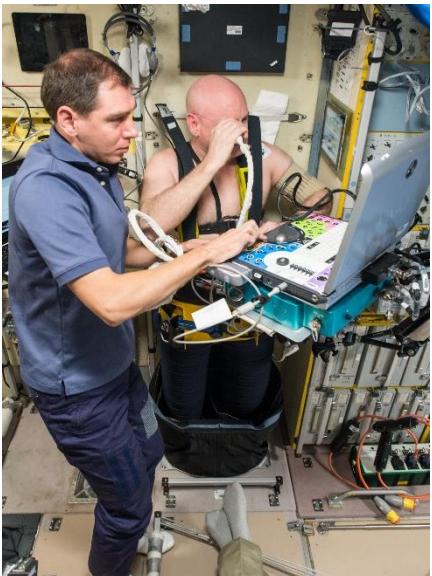


Mathieu E et al 2017



Countermeasures Research

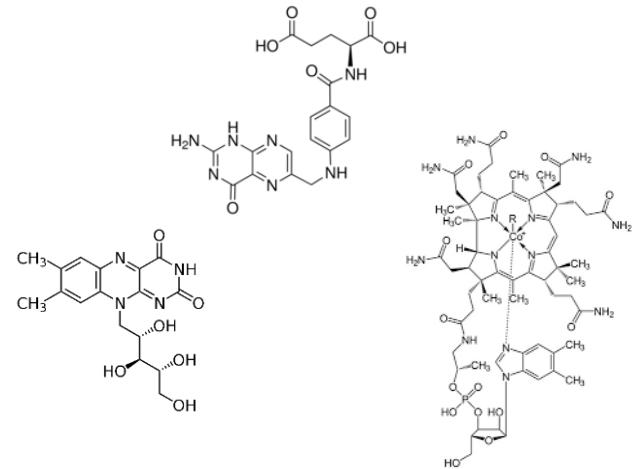
LBNP



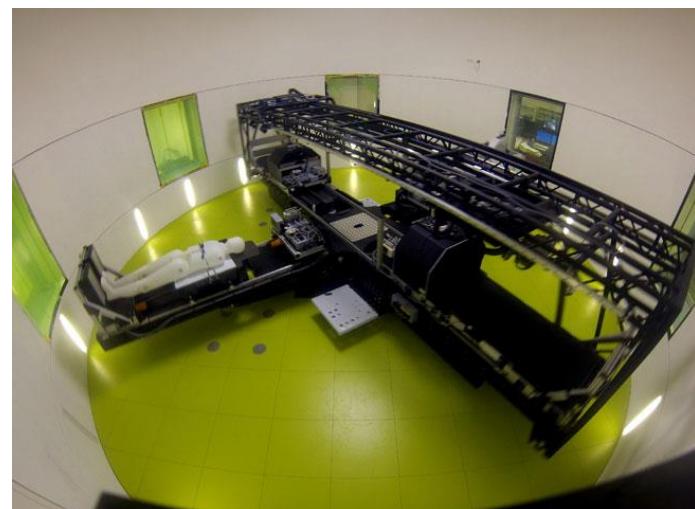
Thigh Cuffs



B vitamins



AG

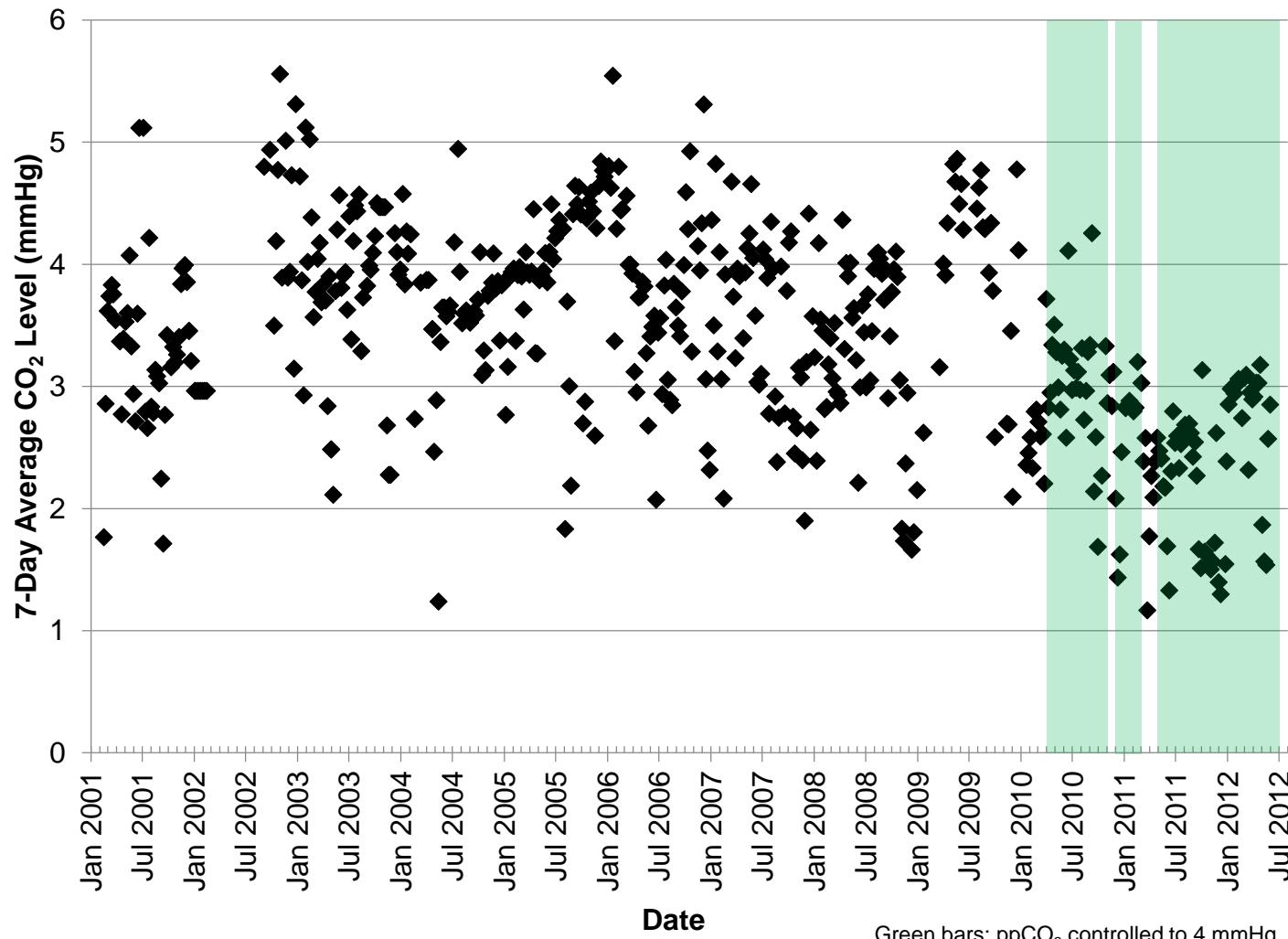


ITD



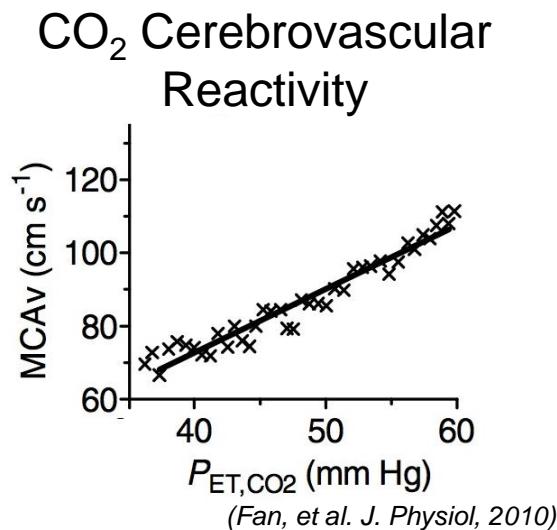


Carbon Dioxide





Carbon Dioxide



Pre-Bed Rest
14 Days
(BR-14 to BR-1)

Ambulatory +
Room Air

Bed Rest
30 Days
(BR1 to BR30)

6° HDT BR +
0.5% CO₂

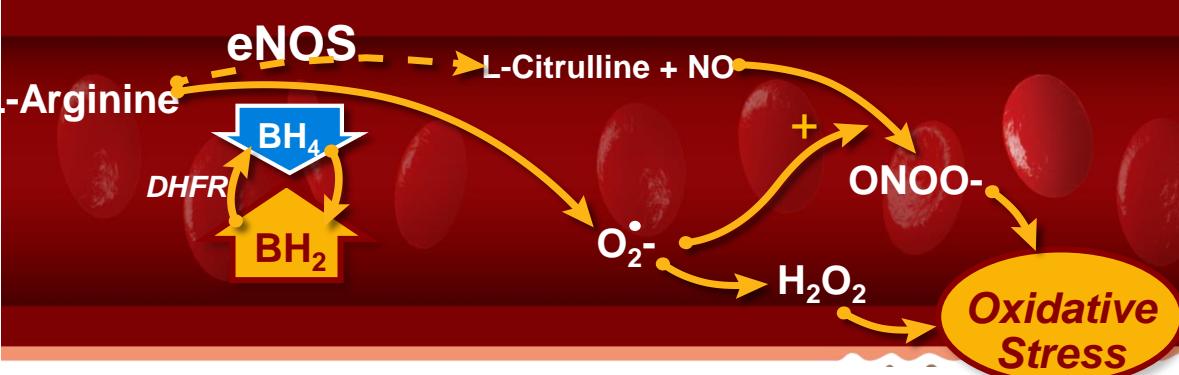
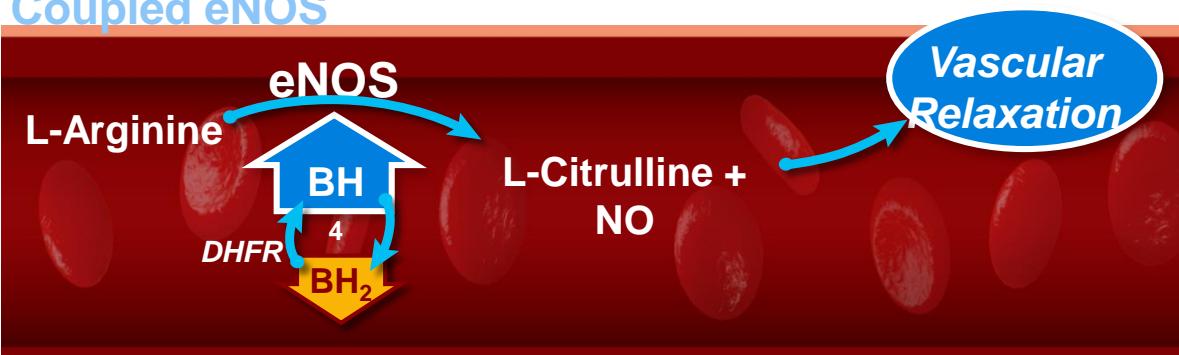
Post-Bed Rest
14 Days
(BR+0 to BR+14)

Ambulatory +
Room Air



Genetics

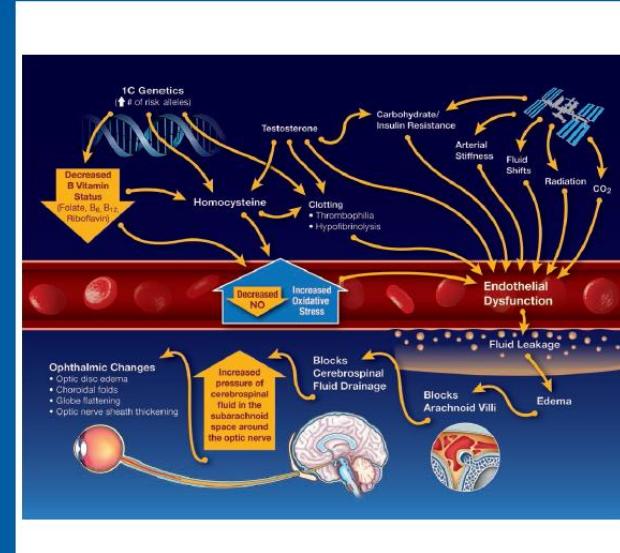
Coupled eNOS



**Uncoupled
eNOS**

THE FASEB JOURNAL

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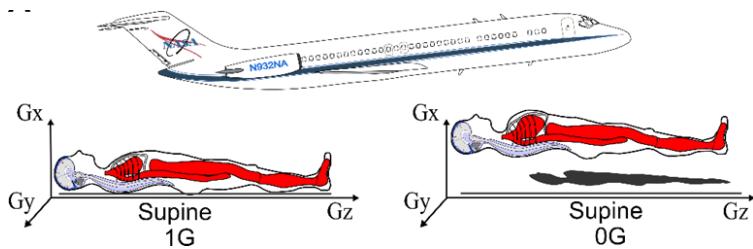
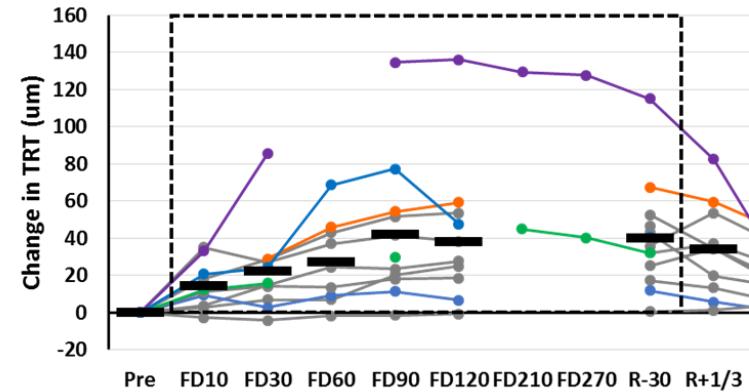
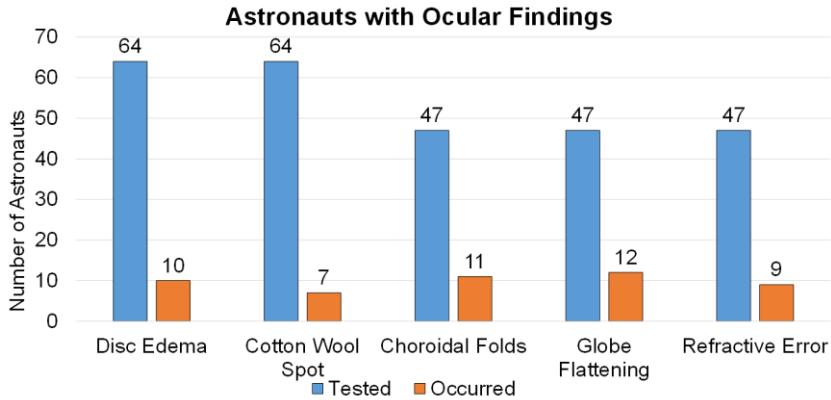


Multiple-hit hypothesis shows how genetics of the enzymes of the 1-carbon metabolic pathway are proposed to be associated with astronaut ophthalmic syndrome. See page 3746.





Summary



B vitamins

